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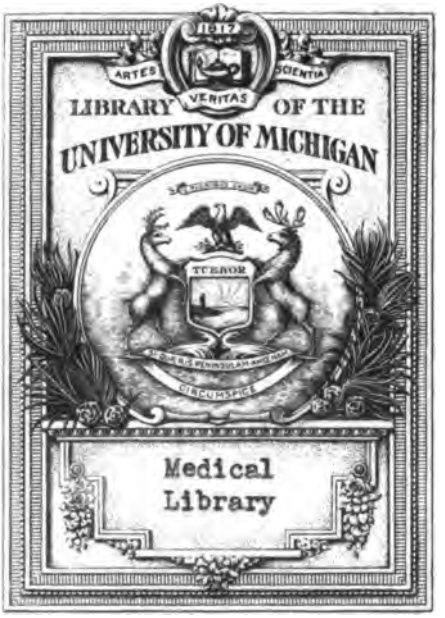

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TRANSACTIONS OF THE

SECTION ON

DERMATOLOGY

of the
American Medical Association
at the Sixty-First Annual
Session, held in St. Louis,
Mo., June 7 to 10, 1910

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LIST OF OFFICERS

This Section was organized in 1887 and has been served by the following officers, the year being the date of election. The list is compiled from the published records, which are incomplete in some cases. It will be appreciated if any errors are brought to the attention of the American Medical Association.

Section on Dermatology and Syphilography

1887 Chairman, L. D. Bulkley, New York City.
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1888 Chairman, L. D. Bulkley, New York City.
Secretary, W. T. Corlett, Cleveland, Ohio.
1889 Chairman, J. E. Atkinson, Baltimore.
Secretary, W. T. Corlett, Cleveland, Ohio.
1890 Chairman, L. D. Bulkley, New York City.
Secretary, W. T. Corlett, Cleveland, Ohio.
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Secretary, J. C. McGuire, Washington, D. C.
1892 Chairman, L. A. Duhring, Philadelphia.
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Secretary, T. C. Gilchrist, Baltimore.
1897 Chairman, A. W. Brayton, Indianapolis.
Secretary, T. C. Gilchrist, Baltimore.

Section on Cutaneous Medicine and Surgery

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Secretary, J. M. Blaine, Denver.
1899 Chairman, L. D. Bulkley, New York City.
Secretary, R. R. Campbell, Chicago.
1900 Chairman, W. L. Baum, Chicago.
Secretary, R. R. Campbell, Chicago.
1901 Chairman, H. W. Stelwagon, Philadelphia.
Secretary, R. R. Campbell, Chicago.
1902 Chairman, John A. Fordyce, New York City.
Secretary, R. R. Campbell, Chicago.
Delegates, M. B. Hartzell, Philadelphia, and William L. Baum, Chicago.
1903 Chairman, Henry G. Anthony, Chicago.
Secretary, R. R. Campbell, Chicago.
Delegate, Jay F. Schamberg, Philadelphia.

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LIST OF OFFICERS—Continued

1904 Chairman, Douglas W. Montgomery, San Francisco.
Secretary, R. R. Campbell, Chicago.
Delegate, A. W. Brayton, Indianapolis.

1905 (The Section did not meet and the old officers acted two years.)

1906 Chairman, R. R. Campbell, Chicago.
Secretary, M. L. Heidingsfeld, Cincinnati.
Delegate, Henry R. Varney, Detroit.

1907 Chairman, M. B. Hartzell, Philadelphia.
Secretary, M. L. Heidingsfeld, Cincinnati.
Delegate, R. R. Campbell, Chicago.

1908 Chairman, William Allen Pusey, Chicago.
Secretary, M. L. Heidingsfeld, Cincinnati.
Delegate, R. R. Campbell, Chicago.

Section on Dermatology

1909 Chairman, Grover W. Wende, Buffalo, N. Y.
Secretary, H. R. Varney, Detroit.
Delegate, William Allen Pusey, Chicago.

1910 Chairman, Charles J. White, Boston.
Vice-Chairman, Martin F. Engman, St. Louis.
Secretary, H. R. Varney, Detroit.

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PROCEEDINGS OF THE SESSION

Tuesday, June 7—Afternoon

The Section was called to order at 2 p. m. in Odeon Recital Hall by the Chairman, Dr. Grover W. Wende, Buffalo, who delivered an address on "Dermatology in General Practice."

Dr. Frank Crozer Knowles, Philadelphia, read a paper on "Purpura Caused by the Ingestion of the Iodids." Discussed by Drs. Howard Fox, New York; J. A. Fordyce, New York, and F. C. Knowles, Philadelphia.

Dr. Alfred Schalek, Omaha, Neb., read a paper on "Pemphigus Foliaceus. Report of a Case." Discussed by Drs. M. McMahon, Palmyra, Ill.; H. H. Hazen, Washington, D. C.; E. S. Lain, Oklahoma City, and A. Schalek, Omaha, Neb.

Dr. Charles J. White, Boston, read a paper on "Alopecia." Discussed by Drs. William O. Roop, Dayton; Frank C. Knowles, Philadelphia; J. M. King, Nashville; Alfred Schalek, Omaha; J. B. Kessler, Iowa City; Isadore Dyer, New Orleans; M. L. Heidingsfeld, Cincinnati; William Frick, Kansas City; William A. Pusey, Chicago; J. Grindon, St. Louis; J. B. Kessler, Iowa City, Iowa; Frances Rowley, Galveston, Tex., and C. J. White, Boston.

Dr. William Frick, Kansas City, Mo., read a paper on "Dermatitis Exfoliativa." Discussed by Dr. Frank C. Knowles, Philadelphia.

Drs. William T. Corlett and Harold Newton Cole, Cleveland, presented "A Report of Three Epidemics of Anomalous Scarlet Fever." Discussed by Dr. W. L. Baum, Chicago.

The Chairman named the following Nominating Committee: Drs. Charles J. White, W. L. Baum and Howard Fox.

Wednesday, June 8—Morning

This was a clinical meeting.

Dr. R. P. Price, Nevada, Mo., presented two cases of pellagra from the Missouri State Hospital No. 3. These cases were discussed by Drs. A. Ravogli, Cincinnati; James W. Babcock, Columbia, S. C.; William T. Corlett, Cleveland; J. W. King, Nashville Tenn., and John D. Long, Washington, D. C.

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Wednesday, June 8—Afternoon

The following five papers were read and discussed as a Symposium on Cancer:

Dr. Leo Loeb, Philadelphia: "The Present Status of the Etiology of Malignant Growths of the Skin."

Dr. John A. Fordyce, New York: "Pathology of the Malignant Growths of Epithelial Tissue," with lantern-slide demonstrations.

Dr. F. B. Mallory, Boston: "Pathology of Malignant Diseases of Non-Epithelial Formation," with lantern-slide demonstrations.

Dr. Joseph C. Bloodgood, Baltimore: "Surgical Treatment of Cutaneous Malignant Growths."

Dr. William Allen Pusey, Chicago: "Treatment of Malignant Growths of the Skin from a Dermatologic Standpoint."

These five papers were discussed by Drs. E. R. LeCount, Chicago; G. W. Jobling, Chicago; F. B. Mallory, Boston; J. W. Vaughan, Detroit; Willy Meyer, New York; William T. Corlett, Cleveland; A. Ravogli, Cincinnati; J. A. Fordyce, New York; J. C. Bloodgood, Baltimore, and W. A. Pusey, Chicago.

On motion of Dr. Corlett, a vote of thanks was extended to those who had participated in this symposium, and especially to those who were not members of the Section.

On motion the election of officers, scheduled for Thursday morning, was postponed until the afternoon session.

Thursday, June 9—Morning

This was a clinical session.

Dr. George A. Zeller, superintendent of the State Hospital at Peoria, Ill., presented a number of pellagra cases. Discussed by Drs. James W. Babcock, Columbia, S. C.; Marcus Haase, Memphis, Tenn.; Tinsley Browne, Hamilton, Mo.; Oliver S. Ormsby, Chicago; Howard Fox, New York; Isadore Dyer, New Orleans, and A. J. Vance, Harrison, Ark.

On motion of Dr. William A. Pusey, Chicago, as amended by Dr. M. L. Heidingsfeld, Cincinnati, a vote of thanks was unanimously extended to the Board of Administration of the State of Illinois and to the Board of Governors of the Missouri State Hospital No. 3, at Nevada, Mo., for their kindness and interest in sending a number of pellagra patients to this meeting, where they had afforded unusual opportunity for the study and investigation of this very important subject; also to Drs. Zeller, Lamson, Price and Babcock and others, who had assisted in this valuable presentation.

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THURSDAY, JUNE 9—AFTERNOON

Dr. J. F. Waugh, Chicago, presented a paper on the "Results of Experience with the Noguchi Modification of the Wassermann Serodiagnosis Test for Syphilis."

Dr. B. C. Corbus, Chicago, read a paper entitled "Two Years' Experience with the Wassermann Reaction in Practice, being a Preliminary Report on Fifty-seven Cases Treated from the Standpoint of the Wassermann Reaction."

These two papers were discussed by Drs. J. Grindon, St. Louis; M. L. Heidingsfeld, Cincinnati; J. A. Fordyce, New York; William Litterer, Nashville, Tenn.; W. T. Corlett, Cleveland; Alfred Schalek, Omaha; E. H. Martin, Hot Springs, Ark.; Edward Bowe, Jacksonville, Ill.; Oliver S. Ormsby, Chicago; V. J. Cohenour, Joliet, Ill.; J. F. Waugh, Chicago, and B. C. Corbus, Chicago.

Owing to the illness of Dr. Howard Fox, he was unable to read his paper on "The Year's Progress in Our Knowledge of Syphilis," so, by unanimous vote, in accordance with the By-Laws, it was ordered read by title.

On recommendation of the Nominating Committee the following officers were elected for the ensuing year: Chairman, Charles J. White, Boston, Vice-Chairman, Martin F. Engman, St. Louis; Secretary, H. R. Varney, Detroit; Delegate, J. A. Fordyce, New York.

Dr. O. H. Foerster, Milwaukee, read a paper on "Primula Dermatitis." No discussion.

Dr. Marcus Haase, Memphis, read a paper on "A Chronic Itching Papular Eruption of the Axilla, Pubes and Breast." Discussed by Dr. J. A. Fordyce, New York.

Drs. Isadore Dyer and Ralph Hopkins, New Orleans, presented a paper on "The Diagnosis of Leprosy." Discussed by Drs. J. Grindon, St. Louis; A. Ravogli, Cincinnati; Marcus Haase, Memphis; S. T. Darling, Ancon Hospital, Canal Zone; William Litterer, Nashville, and Isadore Dyer, New Orleans.

Dr. Oliver S. Ormsby, Chicago, read a paper on "Lichen Planus Atrophicus (Hallopeau)." No discussion.

Dr. M. L. Heidingsfeld, Cincinnati, presented a paper on "Hairy Tongue," with lantern-slide illustrations. No discussion.

Dr. Richard L. Sutton, Kansas City, Mo., read a paper on "Lichen Nitidus." Discussed by Drs. J. A. Fordyce, New York, and R. L. Sutton, Kansas City, Mo.

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On motion, in accordance with the By-Laws, Dr. C. S. N. Hallberg's paper on "The U. S. Pharmacopeia and the National Formulary in Dermatologic Practice" was read by title.

On motion of Dr. M. L. Heidingsfeld, Cincinnati, a vote of thanks was extended to the retiring Chairman and to the Secretary for their efficient services; also to the members of the Section living in St. Louis for their kind entertainment, and their efforts which had resulted in making this one of the most successful meetings in the history of this organization.

Friday, June 10—Morning

This was a clinical meeting, devoted to the presentation of patients and specimens.

Dr. R. H. Davis, St. Louis, showed a case for diagnosis, possibly syphilis of the face. No discussion.

Dr. Davis also showed a case of bromid eruption of the leg. Discussed by Drs. Oliver S. Ormsby, Chicago; Frank C. Knowles, Philadelphia; J. M. King, Nashville; Julius Grinker, Chicago; and R. H. Davis, St. Louis.

Dr. Martin F. Engman, St. Louis, showed a case of hypertrophic lupus in a negro boy. No discussion.

Dr. Engman showed a case of blastomycotic dermatitis. Discussed by Drs. A. Ravogli, Cincinnati; J. B. Kessler, Iowa City; John D. Seba, Bland, Mo.; J. M. King, Nashville, and Engman.

Dr. Engman showed a case of keratosis follicularis (Darier). Discussed by Dr. F. C. Knowles, Philadelphia.

Dr. Engman showed a case for diagnosis. Discussed by Drs. Alexander S. Wolf, St. Louis; William T. Cortlett, Cleveland; and H. H. Hazen, Washington.

Dr. Engman showed a case of mycosis fungoides. Discussed by Dr. Howard Fox, New York.

Dr. W. H. Mook, St. Louis, showed a case of epidermolysis bullosa and one of vitiligo. The latter was discussed by Dr. Frank C. Knowles, Philadelphia.

Dr. William W. Graves, St. Louis, showed a number of boys with scaphoid scapula and made some remarks on the subject. Discussed by Drs. A. Jacobi, New York; Ira C. Chase, Fort Worth; Alfred Saenger, Hamburg, Germany; A. Ravogli, Cincinnati; Julius Grinker, Chicago; Albert E. Sterne, Indianapolis; and W. W. Graves, St. Louis.

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Dr. R. H. Davis, St. Louis, showed the specimen of a case of congenital ichthyosis.

Drs. Martin F. Engman and W. H. Mook, St. Louis, showed cases of onychia; scleroderma; multiple benign cystic epithelioma; mycosis fungoides; lymphangioma circumscriptum; xanthoma diabeticorum; mycosis fungoides; acne excoriativa; xanthoma planum; and a large papillomatous nevus treated with carbon dioxid snow.

The following photographs were exhibited:

PHOTOGRAPHS EXHIBITED BY DR. JOHN A. FORDYCE

CLINICAL

SYPHILIS:

Multiple (3) initial lesions of the lip.
Scar and milia following initial lesion of chin.
Papulo-pustular syphilide of trunk (2).
Follicular syphilide.
Large papular syphilide with chancre of tonsil.
Grouped papular and ulcerating syphilide of back.
Nodular syphilide of lip and face.
Relapsing nodular syphilide of arm.
Large papular syphilide face and body.
Small papular and corymbiform syphilide of back.
Grouped papular syphilide and acne of back.
Scaling syphilide of palm. Group of six cases.
Tubercular syphilide involving greater portion of back.
Serpigenous syphilide of pubic region.
Rupial lesions of body and split papules at angles of mouth.
Syphilis en nappe in groin about broken down gland and papular syphilide of body.
Abscesses of buttocks from intramuscular injections in a cachectic subject.
Multiple gummata of the thyroid.
Multiple gummata of face, throat and larnyx.
Keloidal scars on trunk and extremities following ulcerating lesions.
Deformity of ear after syphilitic ulceration.
Multiple ulcerations and cellulitis of leg.
Syphilitic ulcer and necrosis of ankle.
Syphilitic ulceration of the knee.
Multiple syphilitic ulcerations involving entire front and sides of leg.
Syphilitic ulceration of leg—hereditary.
Ankylosis of cervical vertebrae following luetic process.

LEPROSY:

Photographs showing anesthetic leprosy in a Chinaman, tubercular leprosy in a negro and ichthyosis-like condition of the skin accompanying leprosy.

Lupus vulgaris (2) of the face.

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Epithelioma—Face (3); back (1); multiple of trunk (1).
Von Recklinghausen's disease (2).
Eczematoid dermatitis (15).
Seborrheic dermatitis (4).
Parapsoriasis.
Lichen planus (4).
Acne (2).
Impetigo contagiosa (4).
Ecthyma post-pediculosis.
Dermatitis herpetiformis (2).
Herpes zoster (3).
Lupus erythematosis (6).
Pemphigus (4).
Sclerodactylia (3).
Chronic α-ray dermatitis of hands.
Onychogryposis of hands in a child 5 years old.
Vegetures, abdomen, in a man.

HISTOLOGIC

Granuloma annulare (2).
Tuberculide (4).
Tuberculosis—early.
Follicular syphilide.
Blastomycosis.
Paraffin acne.
Keratosis pilaris.
Pityriasis rosea.
Seborrheic dermatitis.
Ichthyosis.
Dermatitis factitia.
Mycosis fungoides (2).
Lymphosarcoma.
Fibroma.
Melanoma.
Squamous-celled epithelioma (6).
Basal-celled epithelioma (9).
Cell inclusions (4).
Paget's disease of the nipple and lymphangitis (4).

LIST OF PHOTOGRAPHS PRESENTED BY DR. GROVER W. WENDE

Alopecia syphilitic.
Alopecia areata.
Blastomycosis.
Blastomycosis cutis.
Dermatitis medicamentosa.
Dermatitis herpetiformis.
Dermatitis vegetans.
Epithelioma.
Erythema induratum.
Epidermolysis bullosa congenita.
Eczema.
Favus corporis.

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Impetigo contagiosa circinata.
Leukonychia.
Lichen planus (2).
Nevus verrucosus (2).
Papular and papulosquamous syphiloderm.
Papulotubercular squamous syphiloderm.
Ringworm in a hostler.
Raynaud's disease.
Rhinophyma (2).
Tinea versicolor.
Ulcerative tubercular syphiloderm.
Urticaria pigmentosa.
A case for diagnosis.

LIST OF PHOTOGRAPHS PRESENTED BY DR. WILLIAM ALLEN PUSEY

Coccidioidal blastomycosis (6).
Pellagra.
Nevi treated with solid CO_2 (10).
Parakeratosis variegata.
Hemorrhagic gangrenous eruption from iodism (fatal case in a woman).
Iododerma, fatal case in infant.
Idiopathic atrophy of skin.
Cowpox.
Paget's disease of nipple (2).
Elephantiasis.
Arsenical keratoses of hands.
Arsenical keratoses of hands with epithelioma (same case 14 years later).
Tuberculide.

MICROPHOTOGRAPHS

Monilithrix.
Lepothrix.
Adenoma sebaceum.
Pemphigus bulla.
Bulla from edema.
Vesicle of varicella.
Vesicle of eczema.
Urates in skin.

LIST OF PHOTOGRAPHS EXHIBITED BY DR. FRANK CROZER KNOWLES

Universal alopecia (5).
Epithelioma with keratosis senilis.
Fungating epithelioma.
Syphilis (2).
Dermatitis herpetiformis.
Molluscum contagiosum.
Exfoliative dermatitis.
Pemphigus foliaceous.
Hypertrophic scarring.
Tubercular syphiloderm.

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LIST OF PHOTOGRAPHS SHOWN BY DR. WILLIAM T. CORLETT

COLORED ILLUSTRATIONS FROM LIFE

Pellagra, showing typical lesions on hands and elbow.
Pellagra, showing typical lesions on hands.
Eczema, simulating pellagra. Diseases limited to face and back of hands.
Lupus erythematosus, on side of cheek.
Lupus erythematosus, on face.
Tuberculosis, on back of hands.
Epithelioma, on nose.
Congenital syphilis, large plaques on shoulder and trunk of girl aged 12.

On motion of Dr. William T. Cortlett, Cleveland, a unanimous vote of thanks was extended to the members of the local committee for collecting this valuable clinical material and for the energy shown by the officers of the Section, which had helped to bring this meeting to such a successful close.

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DERMATOLOGY AS A SPECIALTY, AND ITS RELATION TO INTERNAI MEDICINE

CHAIRMAN'S ADDRESS

GROVER W. WENDE, M.D.
BUFFALO

It seems appropriate that my address, as chairman of the Section on Dermatology of the American Medical Association, should be devoted not so much to the refinements of a specialty as to the general and fundamental relations of this specialty to medicine as a whole.

One by one the individual branches of medicine have been cut off the main trunk and cultivated exclusively by specialists. This process of the division of labor was inevitable and indispensable for advance through concentration of effort. But, as in all restricted effort, the very concentration tended to narrowness of observation and loss of perspective that impaired the broadest utilization of the observations made, both for the specialist and for the generalist. The specialist became too much a specialist and lost a capacity for the correlation of the minutiæ of his observations into generalizations. The generalist—and I mean by the generalist the scientific internist as well as the general practitioner—on the other hand, was separated more and more in his understanding and interest by the complexity of the specialty. He not only could not follow the complications and intricacies of the specialties but he had little interest in them, in so far as they remained separated by failure to correlate them with their general causes.

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These considerations apply with exceptional force to the specialty of dermatology, which alone concerns us at present. Dermatology has become so complicated with fine distinctions of terminology and classification that its underlying principles and fundamental relations have been much obscured by the haze of details that has enveloped it.

Is it not proper, therefore, that we as dermatologists should make some effort to bridge the ever-widening separation between our specialty and the field of internal medicine? Should we not attempt to interest ourselves more in the newer generalizations of medicine and to bring the internists into closer touch with ourselves and our work? I believe that this is becoming essential to progress. The period of infancy in our specialty is passing. This period has been devoted to the collection of simple observations and facts. This collection cannot be claimed to be completed and must be still further extended. But already the unrelated facts observed and brought together in the domain of dermatology are becoming cumbersome and an impediment to progress. Correlation of these facts must be attempted if confusion is to be avoided. General causes must be sought and discovered. We as specialists alone cannot undertake this difficult task. We must unite with the internists and together work in the clinic and the laboratory in the investigation of broad relations and causes.

With the exception of parasitic and local inflammatory affections of the skin and with the further possible exception of certain skin affections of wholly unknown nature, it may be said that skin diseases are for the most part simply the superficial local manifestations or complications of general or special morbid states involving the tissues of the body either generally or specially in certain organs or groups of organs. In short, most skin diseases are nothing but symptoms or complications of constitutional or special morbid states. This statement may appear at first sight too sweeping

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a generalization and perhaps somewhat of a prophecy, but of its essential truth I have been convinced the more I have given consideration to it.

If I am correct in this view, then my plea for more systematic cooperation between the dermatologist and the generalist is clearly supported. Not only is this cooperation of study demanded for the highest ends of scientific medicine but also for the many incidental advantages to all concerned in it. What needless distress and even disaster ensue to the patient by reason of the ignorance of the general practitioner as to the interpretation of many skin lesions. We as dermatologists are constantly reminded of this fact. Can we claim that the reverse is not also true? How do we know that it is not? With all our little distinctions and refinements of classification of skin lesions do we know much of the internal relations and final causes of these lesions? Do we know that a skilled internist may not discover related manifestations in other parts of the body and suggest therapeutic measures of value equal to or even greater than our own? It is true that, thus far, the internist has added little or nothing to such correlation, because he has failed to realize its value.

But far more important is the determination of new facts, new relations, new conceptions, the simplification of complexity. All these will come in time. We can hasten their coming by stimulating the interest of our fellow internists and working with them.

As dermatologists we should not be summoned to the hospital clinics occasionally and separately to inspect or diagnose an unusual skin affection; we should consult with the internist, give and take, and together learn. Cooperation of study between ourselves and all the departments of scientific research in our hospitals and laboratories should be instituted and systematically prosecuted. How else can dermatology be correlated with scientific medicine?

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It is surprising to note the crude notions still prevalent among the laity and even physicians regarding skin affections. How much harm and needless suffering result from these false views! How many innocent persons are cruelly subjected to unjust suspicions of moral guilt, due to ignorance of the real nature of their skin affections! How frequently do we still encounter such old superstitions as the effect of "catching cold" and of psychic influences in producing all manner of skin diseases!

The idea that skin lesions are manifestations of "impurities of the blood" and require "medicine for the blood" is too deep-rooted in the ignorance and prejudice derived from past teaching to be readily overcome. A natural variation of this view is seen in the notion very commonly held that some skin diseases should not be treated locally, lest they be "driven in." Other variations of the blood diathesis theory still widely held are the views that many skin affections are due to a scorbutic taint or to scrofula.

These are specimens of the theories formerly held by the medical profession and still deeply ingrained in the prejudices of the laity and in the ignorance of many practitioners. Other crude notions of a blood diathesis still persist within the profession, modified, however, to conform with newer conceptions of pathology but still running in the same old grooves. Thus the uric acid diathesis theory of skin affections is nothing but a modern setting of the older views. So long as nothing much was known about uric acid this theory satisfied and was dignified by a certain pseudoscientific assumption of exactness. This idea was handed on to the laity and is to-day one of the chief errors that we have to combat. With the passing of uric acid as a cause of every conceivable ill to which flesh and skin are heir, we shall presently, probably have other variations of the old dogma to contend with. That there may be an element of truth underlying these crude notions we may

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readily believe, for metabolism lies at the foundation of all vital processes and errors of metabolism may be presumed to account for many of the variations from normal in the different tissues and functions of the body. But in making this admission let us not again be led into the same old error of assuming to know the exact nature of such metabolic errors and of assigning to mere hypotheses the dignity of authority. This has been the trouble in the past and warns us of danger in the future. Let us keep in check our enthusiasm for new notions until we can see clearly. Let us contribute our part to the active research now being vigorously pursued in the study of faulty metabolism, but beware of crude generalizations based on incomplete data. Thus only shall we avoid falling victims to the temptation of easy conclusions based on shallow thinking.

But while striving for ideals in the scientific correlation of dermatology with internal medicine, the utilization of the practical knowledge already possessed should not be neglected. How much of practical importance can be contributed to-day by trained dermatologists to general practitioners? How slight is the understanding by most practitioners of the many lesions of the skin which they see! How often do these lesions give important clews to internal affections? The general practitioner must be far better trained in dermatology in order to comprehend and justly to estimate the relations of dermatology to general medicine. A much closer professional relation should exist between the dermatologist and the general practitioner for the good of both and of the patient.

In the short space of this address I cannot consider at length many of the numerous points of practical contact between dermatology and internal medicine, but I may refer briefly to some of them, chiefly for the sake of illustrating the shortcomings in practice resulting from a failure of intimate cooperation between dermatologists and generalists.

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DISEASES ESPECIALLY CALLING FOR COOPERATION BETWEEN DERMATOLOGISTS AND INTERNISTS

Exudative Erythemas.—We have been accustomed to regard as belonging to the specialty of dermatology the several varieties of exudative skin lesions of the erythema group. Only within recent years has this whole complex group been correlated with important manifestations in the internal organs. An appreciation of this correlation is as essential to the dermatologist as to the internist and surgeon. Would it not be folly to treat the skin lesion and to overlook an acute nephritis, bronchitis, pericarditis, arthritis or abdominal complication? Are we, as dermatologists, accustomed to refer such cases for general examination? On the other hand, how rarely do the internist and the surgeon take account of the clew to diagnosis afforded by these lesions in cases presenting acute abdominal symptoms! Twice in a single week I have seen hospital patients barely saved from an unnecessary laparotomy by the timely intervention of physicians who fortunately did possess enough of broad training to embrace a knowledge of the correlation of such skin manifestations with acute abdominal symptoms and to advise against operation. Many instances of laparotomies actually performed for supposed appendicitis, intussusception, twists of the intestines, tumors and other abdominal conditions have been reported—and doubtless many more have not been reported—which could have been avoided by a knowledge of the correlation of such abdominal symptoms with exudative skin lesions of the erythema group. How long will this kind of one-sided specialism continue to the detriment of scientific practice?

Syphilis.—Of all diseases demanding the attention of dermatologists, specialists and generalists, syphilis is one of the most important, involving in its consequences not merely the health and life of individuals but the happiness of families and the welfare of society. This disease, which affects every tissue of the body and re-

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mains transmissible for years and perhaps through generations, first manifests itself by lesions in the skin and mucous membranes, for which the dermatologist is often first consulted. Later, the general practitioner is required to treat the disease for the involvement of internal organs, the neurologist for the late consequences on the nervous system, the surgeon for destructive changes in the bones and joints, and the other specialists in turn for the involvement of various organs. How important it is that this disease be understood in its broadest relations, its various manifestations mastered by all practitioners of whatever limitation in their field of work, and its proper treatment thoroughly comprehended! How far are we from this accomplishment! Dermatologists, by their unusual opportunities for observation of the skin manifestations of this disease, have acquired a skill in its diagnosis that is equalled by no other practitioner. Yet how frequently is our cooperation sought by our colleagues in their doubtful cases? In no other common disease is the penalty exacted for incorrect diagnosis and faulty treatment so severe.

Better education regarding the prevalence, manifestations, diagnosis and treatment of this disease is imperatively demanded. The general ignorance of the medical profession regarding syphilis is deplorable and a reproach that we should feel. A systematic campaign of education in syphilis might well be undertaken by the official organ of our association. To this end I would recommend that our Section take appropriate action.

Leprosy.—This is a disease fortunately rare in this country and for this very reason one that is usually mistaken for other affections, notably for syphilis. Most of its manifestations, however, are found in the skin or external portions of the body, rendering its diagnosis easy for those skilled in lesions of the skin. The training of the dermatologist especially equips him for the differentiation of this disease from those conditions with which it might readily be confused.

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Pellagra.—This disease, which is now attracting so much attention and which has until recently been entirely overlooked in this country, would be readily recognized by any competent dermatologist by reason of the characteristic pigmentation of the skin.

Diabetes.—To a dermatologist such symptoms as slight, recurring inflammation of the prepuce, itching of the skin, ulceration at the base of a nail and furunculosis would at least arouse a suspicion of diabetes; the occurrence of certain skin lesions, xanthoma diabeticorum, would be almost pathognomonic. In diabetes early diagnosis and treatment are certainly important.

Punctate Telangiectases.—These little lesions, while often of no moment, are not infrequently observed in connection with cardiac and hepatic disease and should never be passed over as of no significance without examination of the internal organs.

Eczema and Psoriasis.—While these common affections cannot usually be definitely associated with internal disturbances, not infrequently they can be, and their occurrence should always suggest a careful general examination. Their correct treatment very frequently demands the treatment of the underlying or associated conditions.

Parasitic Skin Diseases.—These wide-spread and annoying diseases of the skin are usually treated by the general practitioner, who has very frequently failed to do his full duty toward them, by reason of incorrect diagnosis, careless methods of treatment and still more careless methods of enforcing personal and public hygiene and quarantine. Errors in any of these points may lead to epidemics that could have been prevented by the institution of proper measures at the outset. These diseases should be among those required by law to be reported and controlled by the public health authorities through the enforcement of suitable quarantine.

Eruptive Fevers.—No class of diseases is of such importance for the public welfare as these. Once started

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they become epidemic and a veritable scourge to the community. Their correct and early diagnosis is, therefore, vital to the protection of the public health. While the diagnosis is often well made by the general practitioner, how frequently is this not the case? Lack of sufficient instruction on these diseases in the medical schools leaves the young graduate poorly equipped to diagnose them. How many medical students ever saw a case of smallpox? What wonder is it, therefore, that in actual practice smallpox is rarely diagnosed until it has already become epidemic and disseminated far and wide?

Both smallpox and scarlet fever are diseases that very frequently appear in individual cases in abortive or anomalous forms, calculated to deceive all but the elect. The general practitioner must be on guard against making fatal errors of diagnosis in such cases and would receive a genuine service from the counsel of an experienced dermatologist when in doubt in his diagnosis.

Drug Eruptions.—The recognition of drug eruptions is important both for their relief and especially for their correct differentiation from more serious conditions with which they are likely to be confused. Imperfect knowledge regarding these common conditions has often led to the gravest diagnostic and therapeutic errors. For example, the coal-tar preparations so widely used often produce eruptions of most varied form and extent in the skin and mucous membranes. Such eruptions have frequently been mistaken for syphilis, lichen ruber, pemphigus, scarlet fever, measles, etc., and in consequence the patient has been subjected to the most unnecessary treatment and restrictions. The correct diagnosis in many such instances has been suggested only by the subsequent repeated occurrence of similar outbreaks of the skin whenever the particular drug has been taken. Every physician should be familiar with the possible cutaneous effects of the drugs which he prescribes, and this knowledge can be acquired only by a large experience

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and exact observation. These eruptions are as a rule well known to dermatologists and should offer little difficulty of diagnosis.

The relationship of the functions of the skin to those of internal organs are beginning to be fairly well comprehended, although many of the most important bearings are still poorly understood. The connection of cutaneous diseases with inflammation of the mucous membranes in some cases is of unusual interest. It is not uncommon for a patient to seek out a physician, bringing the information, during an acute attack of his eczema, that an asthma from which he has suffered shows amelioration, and *vice versa*.

There is another class of cases of skin involvement in which the underlying causes are vasomotor in origin, without recognizable heart lesions, although, in certain instances, the symptom of tachycardia may be present. These circulatory disturbances may be accompanied by a great variety of skin manifestations whose relations to them are as yet but poorly understood.

This list could be extended almost indefinitely, but my purpose will have been effected if the few illustrative conditions cited shall have helped a little to indicate some of the points of contact between dermatology and general medicine and to encourage a closer cooperation of study and effort among all. Our fields of work must remain more or less differentiated, yet should be united more and more by bonds of allegiance and common purpose in the pursuit of ideals in the science and art of medicine.

In the furtherance of these ideals more intimate relations should be cultivated among the special Sections in the meetings of the American Medical Association, so that each Section may have a greater educative influence on the whole body. With this end in view the program of our Section ought to be arranged to include subjects of general interest, that will instruct all. It is hoped

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that the slight attempt in that direction this year may be an inspiration for greater future endeavor.

It is gratifying to me to be the first to welcome this Section under its new designation of the Section on Dermatology. I am sensible of the great honor you have conferred in choosing me as your chairman, and desire to express to you my dutiful thanks and to assure you of my liveliest appreciation. I also wish to acknowledge my indebtedness to our Secretary for his proverbial zeal and energy in connection with the interests of the Section.

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PURPURA CAUSED BY THE INGESTION OF THE IODIDS

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PHILADELPHIA

Because of the numerous types of eruption that may be produced by the ingestion of the iodids the subject is fraught with the greatest interest. Very few lesions of the skin have not been caused, at one time or another, by small or large doses of iodin or its various salts. Hundreds of papers have been written on the subject as a whole or on some interesting phase of it. The literature is so large that I am compelled to limit my remarks to the eruptions of the purpuric type.

Although it is frequently difficult to ascertain accurately its past history in medicine, Coindet[1] was apparently the first to introduce iodin into the practice of medicine as a therapeutic agent. Ricord,[2] in 1839, mentioned various cutaneous eruptions that were caused by the ingestion of potassium iodid; the same author,[3] in 1842, referred to several cases in which he had seen the same drug produce a "veritable purpura hemorrhagica"; the purpuric eruption not having been mentioned in his first communication. Zeissl[4] stated that he had seen in very rare cases ecchymoses and telangiectases in the form of nevi, of the size of the head of a pin, produced by the administration of the salts of iodin. Cazenave[5] was the first to record the occurrence of

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bullous lesions, with sanguinolent serum, followed by ulcerations difficult to heal, caused by the ingestion of potassium iodid. The most complete papers written on the subject of iodism and the various eruptions caused by the absorption of iodin and its various salts have been compiled by Petitjean[6] and Bradley.[7]

I have been able to obtain references in the literature to eleven bullous and fifty non-bullous cases, all of the hemorrhagic type, exclusive of the two petechial cases reported in the present paper. Mora[8] and Welander[9] have also written papers on this subject, reporting cases of the purpuric type, but I have been unable to consult the articles.

HEMORRHAGIC BULLOUS CASES

Sex.—Four of the cases with hemorrhagic bullæ occurred in women (Pusey,[10] Elsner,[11] Broadbent,[12] Taylor[13]); five in men (Russell,[14] Gottheil,[15] Morrow,[16] Bumstead,[17] McGuire[18]); and two in children, the sex being unspecified (Hudelo and Lebar,[19] Hallopeau and Lebret[20]).

Age.—The youngest case reported of the hemorrhagic bullous type, occurred in a child of 10 years (Hallopeau and Lebret[20]); another developed under the age of 20 years (Hudelo and Lebar[19]); one patient showed the idiosyncrasy at 28 years (Bumstead[17]); another at 39 years (Broadbent[12]); one patient was attacked at 45 years (Gottheil[15]); another at 49 years of age (Elsner[11]); one at 50 years (Morrow[16]); one at 51 years (McGuire[18]); and the ninth, at 68 years of age (Russell[14]). The ages of two of the patients were not mentioned (Pusey,[10] Taylor[13]).

Cause of Administration.—In four of the eleven cases, the drug was administered for syphilis (Bumstead,[17] Gottheil,[15] Hallopeau and Lebret,[20] Hudelo and Lebar[19]); in pneumonia (McGuire[18]); in Bright's disease (Broadbent[12]); for rheumatism (Russell[14]); for a "cold" (Elsner[11]); and in three cases the disease for

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which the drug was prescribed was unspecified (Morrow,[16] Taylor,[18] Pusey[10]).

Length of Administration and Quantity of Drug Given.—The quantity of the drug and the length of administration varied considerably in the eleven cases with sanguinolent bullæ; in some but a few small doses produced the outbreak while in others hundreds of grains of potassium iodid were ingested before the point of intolerance was reached. In Bumstead's[17] case the eruption appeared after taking three 20-grain doses of potassium iodid; the outbreak was noted in Taylor's[13] case after 1 dram had been ingested; hemorrhagic bullæ appeared on Elsner's[11] patient after nine doses of potassium iodid had been administered, grains four having been given every six hours; McGuire's[18] patient took a total of 20 grains of the ammonium iodid in 1¼-grain doses; the eruption appeared in Broadbent's[12] case after taking potassium iodid in 3-grain doses during a period of five days; Pusey[10] prescribed for his patient 7½ to 10 grains of potassium iodid three times daily; Russell's[14] patient took 15 grains of iodin in three days; Morrow's[16] patient received 900 grains of potassium iodid in the space of ten days; Gottheil[15] administered 100 grains of potassium iodid daily for six days; Hallopeau and Lebret[20] produced the eruption experimentally on giving 3 gm. of potassium iodid. The dose or the quantity of the drug prescribed was not mentioned by Hudelo and Lebar.[19]

Character of Eruption.—The eruption was multiform, chiefly, however, consisting of hemorrhagic bullæ in Morrow's[16] case. Gottheil[15] recorded the presence of hemorrhagic vesicles and bullæ. Hemorrhagic bullæ with subsequent ulcerations were noted in three cases (Taylor,[18] Russell,[14] McGuire[18]). Pusey[10] reported the occurrence of sanguinolent bullæ, ulcerative and gangrenous areas in his case. In Bumstead's[17] case purpuric spots, clear and hemorrhagic bullæ, and ulcerations were all present. Elsner[11] recorded the presence in his

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patient of hemorrhagic and clear vesicles and bullæ, wheals, and nodular lesions. Hallopeau and Lebret[20] reported a remarkable case, in which hemorrhagic vesicles and bullæ, macular petechiæ, infiltration plaques, papillomatous lesions, and callous areas were produced by the ingestion of potassium iodid. Hudelo and Lebar's[19] patient exhibited large ecchymotic areas, small petechiæ, hemorrhagic bullæ, and a tuberculid of an angiokeratoma type was also present.

Distribution.—The arms, the hands, the face and the legs were attacked in the cases of Broadbent[12] and Gottheil.[15] The lesions were limited to the face, the hands, and the forearms in Morrow's[16] and Elsner's[11] cases. The feet, the lower legs, the face and the hands were involved in Bumstead's[17] patient. Taylor[13] noted the eruption on his patient on the face, the arms and the gluteal region. The face, the shoulders, the groins, the back, and the scalp were attacked in McGuire's case.[18] The face, the scalp, the neck, the chest, the arms and the legs were involved in Russell's[14] case. Hudelo and Lebar[19] reported the involvement of the arms, the neck, the legs and the feet. The distribution was generalized in the case reported by Hallopeau and Lebret.[20] Pusey[10] did not mention the distribution of the eruption.

PURPURIC NON-BULLOUS CASES

Sex.—Ten cases occurred in patients of the female sex (Fournier,[21] Cruveilhier,[22] Silcock,[23] Walter Smith,[24] Morrow,[25] Janovsky,[26] Labat,[27] Waren Tay,[28] Barlow,[29] Raymond[30]); twenty-two developed in the male sex (Ringer,[31] Debuchy,[32] Robinson,[33] Bradbury,[34] Duckworth-Gee,[35] Bernart,[36] Fournier,[21] and Suchanek,[37] each two cases, Ricord,[3] Duffy,[38] Barton,[39] Neumann,[40] Petitjean,[41] Payen,[42] Lemoine,[43] J. H. Wilson,[44] Colcott Fox,[45] Abbe,[46] Hoening,[47] Vidal[48]); and the sex in eighteen cases was not specified (Mackenzie,[49] Petitjean,[50] Virchow,[51] Neumann,[52] Pernet,[53] two cases, Fournier,[21] twelve cases).

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Age.—The youngest case reported occurred in a child of 5 months (Mackenzie[49]). Ringer[31] reported a case at 17 years; Janovsky[26] one at 22 years; Petitjean's[41] was noted at 23 years of age; Suchanek's[37] patient developed the eruption at 24 years; Duffy's[38] patient showed the outbreak at the twenty-fifth year; the case of Duckworth-Gee[35] developed at 29 years; four cases were recorded at 30 years of age (Fournier,[21] Neumann,[40] Colcott Fox,[45] Abbe[46]); Bernart,[36] reported a case at 31 years; Lemoine's[43] occurred at 32 years; Barton,[39] noted his case at 35 years; Walter Smith[24] observed his patient at 39 years; the outbreak developed in Barlow's[29] patient at the forty-second year; Labat's[27] case showed the exanthem at the forty-third year; the eruption appeared in Waren Tay's[28] patient at the age of 44 years; the outbreak in Suchanek's[37] second patient occurred at the forty-sixth year; the eruption appeared in Vidal's[48] case at 50 years of age; a case reported by Raymond,[30] developed at 53 years; Bradbury's[34] patient was 58 years old when the eruption appeared; the outbreak attacked Robinson's[33] patient at 53 years of age; Hoenning reported the case of the oldest patient (aged 64) in whom the eruption appeared. The age of the patients on whom eruption of petechiæ and ecchymoses developed were not mentioned by Fournier,[21] fourteen cases, Pernet,[53] two cases, Ricord,[3] Cruveilhier,[22] Silcock,[23] Petitjean,[50] Morrow,[25] Payne,[42] J. H. Wilson,[44] Neumann,[52] Virchow,[51] Debuchy.[32]

Cause of Administration.—The drug was administered for syphilis in eighteen cases (Bernart,[36] Fournier,[21] three cases, Cruveilhier,[22] Silcox,[23] Suchanek,[37] two cases, Walter Smith,[24] Petitjean,[50] Janovsky,[26] Payen,[42] Barlow,[29] Colcott Fox,[45] Abbe,[46] Hoening,[47] Vidal,[48] Mackenzie,[49]). It was given in the treatment of rheumatism in eight cases (Duffy,[38] Labat,[27] Lemoine,[43] J. H. Wilson,[44] Raymond,[30] Bradbury,[34] Ringer[31] Debuchy[32]). The iodid was given in one case

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for paralysis (Barton[39]); for leprosy in another (Pernet,[52]) for atrophy of the optic disc in a third (Waren Tay[28]); for uratosis in one case (Robinson[33]); and in another for cancer (Virchow[51]). The indication for the use of the drug was not specified in nineteen cases (Fournier,[21] twelve cases, probably given for syphilis, Duckworth-Gee,[35] Ricord,[3] Petitjean,[41] Pernet,[53] Morrow,[25] Neumann,[40, 52] two cases).

Length of Administration and Quantity of Drug Given.—Mackenzie[49] described a case in an infant of 5 months in which the eruption appeared in three-quarters of an hour, after 2½ grains of potassium iodid had been given. In Colcott Fox's[45] case the eruption developed after two doses of 5 grains each, of potassium iodid had been administered about six hours apart. Three 5-grain doses of potassium iodid caused the outbreak in the case reported by J. H. Wilson[44]. In Robinson's[33] case potassium iodid was given in grain doses three times daily; the eruption occurred after six days of medication. The outbreak appeared in a few days in Labat's case[27] after giving 3-grain doses. Lemoine[43] prescribed 1 gm. of sodium iodid daily; the next day the eruption appeared, twenty hours after the drug was administered. Ringer[31] gave his patient 10 grains of potassium iodid three times each day; the rash appeared in five days. Waren Tay[28] produced the eruption on prescribing 1.5 gm. of potassium iodid daily. Petitjean[50] gave between 3 and 4 gm. of potassium iodid daily; the outbreak occurred in four days. Abbe[46] prescribed 10 grains of potassium iodid three times daily; the eruption appeared after two weeks' administration. Raymond[30] gave 50 cg. of potassium iodid in two doses daily; after ten days the dose was increased to 1 gm. daily; the outbreak occurred after 8 gm. of the drug had been ingested. In Vidal's[48] case 15 grains of potassium iodid were given three times each day; the exanthem appeared after the drug had been taken for three weeks. Barlow[29] ordered 1 gm. of the drug to be given daily;

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at about the third week the potassium iodid was increased to 1.5 gm. each day; two days later the rash developed. The eruption appeared in Janovsky's case[26] after 24 gm. had been administered; 2 gm. sodium iodid having been given daily. Hoening[47] prescribed a mixture of sodium and potassium iodids; 40 gm. of this combination were given in twenty days. Silcock[23] gave 10 grains of potassium iodid three times a day; the dose was increased after fifteen days to 15 grains three times daily; seven days later the eruption appeared. Duffy[38] prescribed for his patient 10 grains of potassium iodid three times each day; the dose was increased three weeks later to 15 grains three times daily; 2½ ounces of the drug were given; the outbreak occurred in one month's time. Suchanek[37] gave a total of 42 drams in one case and 23 drams of potassium iodid in the other. In Duckworth-Gee's[35] case 50 cg. were given daily; 6 gm., in all, were ingested. In Payen's[42] case the eruption appeared after two months treatment with the iodid of iron. The eruption occurred after administering potassium iodid for five days in Bernard's case.[36] Moderate doses of potassium iodid were given in Fournier's[21] three cases; the purpuric spots appeared in one week, five days, and a few days, respectively. The rash appeared after a few doses in Debuchy's case.[32] The outbreak occurred in Ricord's[3] case after potassium iodid had been given for fifteen days. After the drug had been given but a few days the exanthem appeared in the case reported by Walter Smith.[24] The eruption appeared on Barton's[39] patient in three weeks' time, small doses of potassium iodid having been prescribed. The dose of the drug and the length of administration were not mentioned in twenty of the cases (Cruveilhier,[22] Neumann[40, 51] and Pernet,[53] each two cases; Petitjean,[41] Bradbury,[34] Virchow,[51] Fournier,[21] twelve cases).

In a few instances the eruption appeared some days after the drug had been discontinued. Suchanek[37] recorded a case in which the eruption appeared eight

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days after the iodid had been stopped. In the hemorrhagic bullous case reported by Morrow[16] the eruption did not reach its height until five days after the potassium iodid had been intermitted. In the case with hemorrhagic bullæ recorded by McGuire[18] the lesions continued to appear for ten days after the drug was discontinued. Broadbent[12] also recorded the fact in his hemorrhagic bullous case that the eruption continued to appear for six days after the potassium iodid had been stopped. The purpuric exanthem continued to appear for eight days in one of Suchanek's[37] cases, and for twenty-six days in the other. Outbreaks of purpura from the iodid continued for ten days in Janovsky's[26] patient, and for three weeks in Raymond's[30] case.

Type of Eruption.—In all of the non-bullous cases, except five, the eruption was entirely purpuric in type. The lesions were mostly from small to large pinhead in size; in Hoening's[47] case, however, some of the ecchymoses were one-quarter dollar in dimensions. Duckworth-Gee[35] described, in the case reported, a herpetic eruption with a purpuric areola. In Neumann's[40] patient the eruption was chiefly papillomatous or pustular; some of the lesions were petechial. In one of the two cases reported by Petitjean[41], with purpuric lesions, the predominant type consisted of furuncles and pustules. Vidal[48] noted in his case a papular outbreak on the trunk and a purpuric eruption on the legs. The outbreak in Debuchy's[32] case consisted of a vesicular as well as a petechial eruption; an eczema was also present.

Distribution.—The eruption was, in a great majority of the cases, localized to certain portions of the body, chiefly the lower extremities. The eruption was generalized in Hoening's[47] case. The outbreak was generalized, excepting the chest, the back, and the hairy scalp, in Neumann's[40] patient. The upper and lower extremities and the shoulders were attacked in the case reported by Mackenzie.[49] There was extensive involvement in Lemoine's[43] case; the thighs, the abdomen, the lumbar

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region, the chest and the arms are the areas attacked. The entire face, the forearms and the neck were the areas of predilection in Duckworth-Gee's[35] patient. The scrotum, the thighs and the legs were involved in Bernart's[36] case. The upper and lower extremities were attacked in two cases (Janovsky,[26] Bradbury[34]). The forearms and the lower portion of the legs were involved in three cases (Colcott Fox,[45] Abbe,[46] Robinson[33]). Raymond's[30] patient showed the lesions distributed on the arms, the hands and the legs. The hands and the legs were the seats of attack in the case recorded by Debuchy.[32] J. H. Wilson[44] noted the distribution in his patient on the lower legs, and the dorsum of the feet. The eruption was limited to the lower abdomen in one case, and attacked the lower abdomen and the extremities in the other case of Suchanek's.[37] The lower extremities alone were attacked in eight cases (Cruveilhier,[25] Silcox,[23] Barton,[39] Waren Tay,[28] Vidal,[48] Ringer,[31] Petitjean,[41, 50] two cases). The eruption was limited to the lower portion of the legs in twenty cases (Duffy,[38] Ricord,[3] Walter Smith,[24] Payen,[42] Labat,[27] Barlow,[29] Fournier,[21] fourteen cases). In one of Fournier's[21] fifteen cases, the outbreak was not only found on the lower legs but lesions, purpuric in type were also scattered on the trunk. The distribution of the eruption was not specified in five cases (Morrow,[25] Neumann,[62] Virchow,[51] Pernet,[53] two cases).

Mild symptoms of iodism preceded or accompanied the eruption in several of the cases, notably in those reported by Petitjean,[50] Janovsky,[26] Barlow,[29] J. H. Wilson,[44] and Debuchy.[32] Severe symptoms of iodism were observed in Mackenzie's[49] and Raymond's[30] fatal cases.

Edema of the glottis was caused by the drug in two of the cases (Petitjean[50] Neumann[52]). Several authors have referred to edema of the glottis caused by the ingestion of potassium iodid. Nelaton,[54] Lawrie-Adair,[55] and Fenwick[56] have reported cases of this char-

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acter. Weist[57] recorded an interesting history; a woman of 28 was instructed to take 50 grains of potassium iodid a day; eleven hours after the first dose was administered a generalized edema developed.

Mucous Membrane Involvement.—The mucous membranes were attacked in two of the hemorrhagic bullous cases. Hemorrhagic bullæ were found on the tongue and the roof of the mouth in the case reported by Taylor.[18] Russell[14] recorded the occurrence of bullæ filled with blood in the nares in his case. The mucous membranes were attacked in five of the non-bullous petechial cases. Purpuric spots were noted on the left conjunctiva in Duckworth-Gee's[35] patient. A hemorrhagic eruption was present on the gums in the patient of Suchanek.[37] Numerous ulcers were found on the walls of the stomach near the pylorus in Neumann's[52] patient, supposedly caused by the ingestion of potassium iodid. The roof of the mouth exhibited petechiæ in Hoening's patient,[47] and on the hard palate in the one reported by Mackenzie.[49] Milain[58] described a case in which ecchymotic spots were found on the palate, which appeared on starting the drug and disappeared on stopping the same. There was a papulopustular eruption on the face, the back and the limbs caused by the potassium iodid, but there were no purpuric lesions on the cutaneous surface.

Hemorrhage from Mucous Membranes or Organs.—Boinet[59] in 1865 mentioned the fact that the ingestion of iodin may cause hemorrhage from the lungs and the intestines. Rodet[60] recorded an interesting case in which a man of 35 was attacked by hemoptysis whenever potassium iodid was given. DeBolze[61] reported an instance in which a blood-tinged cough was produced whenever the iodids were given; no signs of phthisis were present. Lindsay[62] referred to a case in which a woman of 58 after taking a few doses of potassium iodid developed the catamenial flow, which had been absent for twelve years. This flow continued for the

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entire week during which the drug was given. The administration of the iodid also caused symptoms of iodism and a bullous, non-hemorrhagic eruption.

In the present series two of the hemorrhagic bullous cases and five of the petechial, non-bullous cases exhibited phenomena of this character. Hemoptysis was noted in Broadbent's[12] case. Elsner's[11] patient vomited blood and passed the same by the rectum. Epistaxis and bleeding from the gums were noticed in the case reported by Duckworth-Gee.[35] Cerebral hemorrhage was present in Neumann's patient; whether caused by the drug or from some other condition is not clearly stated by the author. Epistaxis was caused by the drug in the cases recorded by Jańovsky,[26] Bradbury[34] and Abbe.[46]

Organic Disease Present at the Time of Administering the Iodid.—Heart or kidney disease, one or both, were present at the time the drug was administered in four of the cases which developed the hemorrhagic bullous lesions, and in six of the non-bullous cases. Disease of both the heart and kidneys were found in Morrow's[16] and Gottheil's[15] patients. Disease of the kidneys was found in the case recorded by McGuire.[18] Broadbent's[12] case exhibited nephritis, pericardial trouble and a pleuritic condition of the lungs. Nephritis was discovered in the two cases reported by Neumann[40, 52]. Valvular disease of the heart was present in the case recorded by Duffy.[38] Nephritis and valvular disease of the heart were found in Lemoine's[43] and Pernet's[53] cases. Pericarditis, congestion of the lungs, aortic and mitral lesions, hypertrophy of the heart, and disease of the kidneys were all noted in Duckworth-Gee's[35] patient.

CASES OF THE AUTHOR

Case 1.—Helen L., aged 27, born in Germany, came to the skin dispensary of the Pennsylvania Hospital, April 13, 1906. There were no derangements of the heart or kidneys present, and her past history was negative. A few weeks previous to

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her visit to the dispensary she obtained a mixture at a drug store for pains in her muscles and joints. The patient stated that the mixture contained potassium iodid. After taking the preparation for some weeks, ten days before coming to the dispensary an eruption appeared on the lower extremities. The lesions were limited to the lower extremities, extending from the upper thighs to the ankles, and consisted of bluish and reddish-blue, pinhead to split-pea-sized macules, from which the color could not be pressed. The eruption disappeared a few days after stopping the medication. To prove whether or not the iodid was the etiologic factor, one week after the disappearance of the lesions the drug was again given. Potassium iodid was given in 10-grain doses three times daily; on the second day 11 grains were given at a dose, on the third, twelve grains three times during the day, and the administration was continued in the same ratio. When the dose had been gradually raised in this manner to 17 grains three times daily, a purpuric eruption developed with the same characteristics and distribution as the first outbreak, previously described.

CASE 2.—Mary H., a very light mulattress, aged 40, born in North Carolina, came to the skin dispensary of the Pennsylvania Hospital, July 13, 1906. The patient had previously been treated in Dr. Morris Lewis' ward at the Pennsylvania Hospital for aneurism and aortic insufficiency. No history of rheumatism could be obtained. The urine contained no albumin or casts. The patient was given 10 grains of potassium iodid, three times a day. The drug was started April 15 and continued until the patient's visit to the dispensary. A few days before she came to the skin dispensary the eruption appeared on the legs. The purpuric lesions were large, pin-head in size and limited to the tibial aspect of the lower legs. The eruption disappeared a few days after the drug was stopped. One week after the disappearance of the lesions the drug was again given. Five grains of potassium iodid were administered three times daily. After the drug had been taken for twenty days the purpuric eruption again appeared on the same areas as previously exhibited the outbreak.

Potassium iodid is not the only salt of iodin that may produce an eruption, as the outbreak was produced in Lemoine's[43] patient by sodium iodid and also in the case reported by Janovsky.[26] The iodid of iron was causal in Payen's[42] case. The eruption was caused in Hoening's[47] patient by a combination of the sodium

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and the potassium iodids. Both the ammonium and the potassium iodids, separately, produced the outbreak in Duffy's[38] and Ringer's[31] cases. The latter writers however, reported negative results with the sodium iodid.

The same individual may have an idiosyncrasy to more than one drug. Raymond[30] found that his patient had also a marked intolerance for 5 cg. of santonin, and for 2 gm. of sodium salicylate.

Pathology.—Tilbury Fox[63] believes in the follicular and sebaceous gland origin of all types of iodid eruption. Fox and Gibbes[64] found that the small arteries were blocked and the vessels were affected in every section examined by inflammatory changes. Engman and Mook[65] found in the examination of papules, pustules and macules from numerous cases of iodid eruption that the sebaceous glands and the follicles were not primarily affected by the drug, practically all of the changes occurring in the neighborhood of the blood vessels. Thin[66] found in the acne form of eruption, caused by the ingestion of potassium iodid, limited edema with congestion of the vessel; in the bullous or pustular form an effusion of serum with more or less of the formed elements of the blood, and in the purpuric type destruction of the wall of the vessel and hemorrhage. Thin[66] points out the tendency of iodin when present in the blood current to attack special points of the vessels, thus explaining all the varieties of eruption caused by iodin. As an explanation of the purpuric eruption he suggests that a portion of the vessel is so suddenly and completely destroyed that the local changes are limited to effusion of a small quantity of pure blood, and to plugging of the vessel. The specimen examined by Thin[66] showed the changes limited to a small part of the vessel, which was dilated at that spot and blocked by coagulum. Duckworth and Harris[67] found the blood vessels were very numerous in all of the specimens examined. The sebaceous gland

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origin of the various types of iodid eruption can probably be excluded, as most authorities do not agree with the original findings of Tilbury Fox.[68] As Biesiadecki[68] and others have never been able to demonstrate the presence of either sebaceous glands or lanugo follicles on the palms of the hands, and as Duhring[69] and Hyde[70] have each reported eruptions from potassium iodid on this area, the sebaceous origin of the outbreak is evidently disproved.

Absorption and Elimination.—Arnozan and Carles[71] have gathered together in an excellent paper the facts regarding the role the leucocytes play in the absorption of certain medicines, including iodin. The latter phase of the subject has been particularly studied by Stassano and Bourcet.[72] The leucocytes absorb the iodin and carry this drug, with which they are charged, to different tissues or organs of elimination. The drug absorbed may undergo various changes in the leucocytes, being transformed by the action of various ferments which these cells contain. The drugs may be stored by these cells at various points and thus give rise, under various circumstances, to a pathologic effect. Ménière,[73] after a great many experiments, concluded that the time required for the absorption of the salts of iodin and their elimination by the salivary glands is on an average from eight to ten minutes; when the stomach is full the elimination is retarded from thirty to forty minutes. If the stomach is absolutely empty and the potassium iodid is given in a warm liquid of some stimulating power, such as tea, elimination may be detected in the saliva in from two to three minutes. According to this same investigator absorption of this drug occurs most rapidly by the bronchial mucous membrane; it takes slightly less than double the time for absorption to occur by the stomach and the esophagus as by the bronchial mucous membrane. Quincke[74] found the presence of iodin in the small intestine, the

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saliva, the urine, the serum of the blood and in the aqueous humor, but not in the stomach or the large intestine, one and one-quarter hours after a hypodermic injection of the drug had been given; while it took almost two and one-half hours to produce the same results after ingestion through the stomach.

Iodin has been found in the urine in several of the cases in this series, Janovsky[26] noted the reaction for the drug for six days after the medication had been stopped; iodin was found in the urine in Pusey's case.[10] Berg[75] gave a venous injection of from one hundred to one hundred and thirty grains of potassium iodid in animals and iodin was found in the urine after fifteen minutes had elapsed. Marshall[76] recovered 265 grains daily in a case of Wood's, in which 360 grains of potassium iodid were taken daily. According to Sée,[80] the reaction to the drug may exist in the saliva after it has disappeared from the urine.

Adamkiewicz[77] mixed the pus from the pustules caused by the ingestion of the iodid with starch and added a few drops of very dilute nitric acid, and obtained the reaction of iodin. The test for iodin in Gottheil's case proved negative. Engman and Mook[65] in a valuable series of experiments on numerous patients with various types of iodid eruption proved the elimination of iodin through the skin. They found a positive reaction of the pus in every case examined, iodin being distinctly present. Skin free from any lesions, although an iodid eruption was present on other portions of the body, was blistered by them in two cases and the serum from these blisters was investigated. In each instance iodin was readily discovered, thus proving that iodin occurred in chemical combination in all the tissues of the body. Taylor[78] believes that iodin is eliminated in certain cases by the sweat-glands, citing a case to prove this assertion.

Prognosis.—The administration of the iodids, particularly in large doses, to those individuals who have

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a strong idiosyncrasy to the drug, or in cases with organic disease of the heart or the kidneys, is frequently a dangerous procedure. Seven out of the eleven hemorrhagic, bullous cases ended fatally, and two of the non-bullous, petechial type. Elsner's[11] patient died five days after the drug was started! Russell's[14] patient succumbed on the tenth day after the drug was first given. The patient whose case is reported by Pusey,[10] died ten days after the appearance of the eruption. The termination was fatal in Gottheil's[15] case, seventeen days after the medication was commenced. Broadbent's[12] case ended fatally three weeks after the drug had been given on a second trial. Morrow's[16] and McGuire's[18] patients died six weeks after the drug was first administered. Mackenzie's[49] case proved fatal sixty-eight hours after one dose, 2½ grains of potassium iodid, had been given to a child of five months. In Duckworth-Gee's[35] case, the patient died on the tenth day after the drug had been started.

Fournier[21] has had more opportunity to study purpura caused by the ingestion of potassium iodid than any other observer, as he has reported in one series fifteen cases. According to his observations, if the drug is given in the same moderate dose over an uninterrupted period the purpuric eruption produced by the potassium iodid is apt to lessen in severity until there is an almost complete disappearance, even while the small dose of the drug is continuously given; if, however, the dose of the drug is considerably increased, a fresh outbreak will occur which is usually not so severe as the first attack. If the drug is stopped for a few weeks, and the same small dose is given as in the first instance, an eruption will again be produced but the outbreak is usually not so severe as the lesions first caused by this small dose. The experience of Fournier[21] has coincided with the observation of more recent writers on the subject. A certain tolerance, therefore, seems to be formed to the drug in a great many individuals

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who are susceptible to this medication, but the tolerance is but transitory, as the increase of the dose, while the drug is being taken in moderate quantities, will produce a fresh outbreak, or if the drug is stopped for but a few days the tolerance is lost and the original dose, or even a smaller quantity, will again produce the eruption.

The decreased dosage causing the eruption is well exemplified in the bullous, non-hemorrhagic case described by Besnier,[79] in which the outbreak was first caused by 2 gm. of potassium iodid, on a second occasion by 1 gm. and a third time by 10 cg. The eruption was first produced in Duffy's[88] case by 2½ ounces of potassium iodid, and on another occasion by 15 grains. In Abbe's[46] case the eruption was produced on six different occasions, each time less of the drug being required to cause the outbreak; the eruption first appeared after 10 grains of potassium iodid, three times daily, had been given for two weeks; the fifth and the sixth attack was caused by three and by two 5-grain doses respectively. The eruption was at first caused in Raymond's[80] case by giving 8 gm. of the drug, in divided doses, the second outbreak was induced by administering 3 gm. in five days. On the first occasion the exanthem appeared in Ringer's[81] case after 10 grains of potassium iodid three times each day had been given for five days, the eruption was reproduced by prescribing four 10-grain doses of the drug. The outbreak first occurred in McGuire's[18] case after 20 grains of ammonium iodid had been given; on a second occasion 5 grains sufficed to produce the hemorrhagic bullæ. The administration of 1.5 gm., of potassium iodid in Waren Tay's[28] patient produced the eruption on five different occasions in nine weeks. In one of my cases the eruption was reproduced by one-half of the dose of the drug and in one-quarter the length of time required for the first outbreak.

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After a careful study of sixty-three cases of purpura caused by the ingestion of potassium iodid, eleven being of the hemorrhagic, bullous type, I feel justified in making two provisional groups of these eruptions. In the first group may be placed all those cases in which there is some organic disease, some lowered condition of the general economy which makes the individual more susceptible to the effects of the drug, and those with a strong idiosyncrasy to the iodid. The bullous eruptions of the hemorrhagic type and the petechial cases with a somewhat generalized outbreak should be classed in the first group. In the second group the patient is found in the best of health, and there is absolutely no way of explaining the outbreak except on the hypothesis of a mild idiosyncrasy to the drug. In this latter group should be placed the purpuric cases with a very localized distribution, which have the tendency to remain limited, particularly to the lower portion of the legs. Fournier's[21] fifteen cases should be taken as the type of case belonging in the second group. There is probably no doubt that in the localized cases of purpura, caused by the iodids, in which small doses of the drug have been administered, the eruption may be made general and severe if the drug is continued in very large doses over a long period of time. The drug should be used with the greatest care in those individuals with some organic lesion, in whom the general condition is below par, and as a safeguard the beginning dose should be small, as a strong idiosyncrasy to the iodid may be present.

SUMMARY

Purpuric eruptions caused by the ingestion of the iodids may be divided into two provisional groups.

The first group includes the extensive petechial and hemorrhagic, bullous cases, which occur in those individuals with organic disease, particularly of the kidneys or the heart, or with a lowered condition of the general

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economy, making them more susceptible to the effect of the drug, or with a strong idiosyncrasy to the same.

The second group includes all cases with a localized distribution, particularly those in which the eruption is limited to the lower extremities or the lower legs, which occur in those individuals in perfect health, and which can be explained only on the theory that a mild idiosyncrasy to the iodid is present.

Sex and age have nothing to do with the occurrence of the eruption, although most of the cases developed during middle life, and a considerably larger percentage of males were attacked than females.

The drug was administered in twenty-two of the sixty-one cases for syphilis, for rheumatism in nine cases, and in the remainder in numerous other conditions, none of which apparently exerted any predisposing influence.

The quantity of the drug given and the length of administration varied so markedly that an average dose or the length of time of continuance cannot be stated, the personal element alone deciding the question of an eruption.

The eruption was chiefly of one type, either the petechial or the hemorrhagic bullous, although in a few cases other forms of iodid lesions were present.

In the hemorrhagic bullous cases, although in several the eruption was somewhat generalized, the face and the extremities were mostly involved, particularly the face and the arms.

In the petechial type the eruption in a great majority of the cases was limited to the lower extremities, particularly the lower portion of the legs; in a few cases, however, the outbreak was somewhat generalized or noted on the upper as well as the lower extremities.

Mild symptoms of iodism were present in a few cases, and severe reaction to the drug was noted in two cases. Edema of the glottis was found in two instances.

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Lesions were found on the mucous membranes in a few cases; hemorrhages occurred from the mucous membranes or from various organs in a few others.

Organic disease of the kidneys and the heart were found in but few—ten out of sixty-one cases.

The various salts of iodin are all capable of causing a purpuric eruption.

The pathologic changes of the skin were noted in the immediate vicinity of the blood-vessels and in the walls of the vessels themselves.

Iodin is rapidly absorbed by all mucous and serous surfaces and rapidly eliminated, chiefly by the kidneys and also through the skin itself. The leucocytes play a distinct rôle in the absorption of the drug.

Hemorrhagic bullous cases, of extensive distribution, are frequently fatal, seven out of the eleven in this series ending fatally.

Petechial, non-bullous cases rarely terminate in death, unless there is marked disease of the heart or kidneys or a very extreme intolerance to the drug; two out of the fifty cases of this type ended fatally.

In conclusion I wish to express my thanks to Dr. Charles N. Davis for the privilege of reporting the two cases and to make a plea for smaller doses of the iodids.

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ABSTRACT OF DISCUSSION

DR. J. A. FORDYCE, New York: I do not think we ought to allow this occasion to go by without deprecating the reckless way in which potassium iodid is given, not only by the general practitioner, but by the specialist. In syphilis it is frequently given in doses of several hundred grains daily, and in the majority of those cases the same benefit could be derived from thirty, or, at most, one hundred grains daily. We are entirely too reckless in the administration of the drug, and have overlooked the fatalities that have been reported from its excessive use. In some instances, these harmful effects are due to excessively large doses; in others, to an over-susceptibility on the part of the patient. Dr. Knowles' paper also emphasizes the importance of looking into the condition of the eliminative organs before we resort to large doses of potassium iodid.

DR. HOWARD FOX, New York: In connection with this rare form of eruption due to the ingestion of potassium iodid, I should like to call attention to another rare form, a case of which I recently presented before the New York Dermatological Society. The eruption was a very extensive one of the purely bullous type. When the patient, a colored girl of 12 years, came to the Vanderbilt Clinic, she presented a number of unpigmented circinate lesions that we were disposed to regard as dermatitis herpetiformis of the circinate and bullous type. The patient gave a history of having taken five weeks previously a bitter medicine in doses of ten drops three times a day for one week. At the suggestion of Dr. George T. Jack-

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son she was given iodid of potash, ten drops three times a day. After the second dose an eruption consisting of large, tense, clear bullæ appeared on the whole body, more especially on the legs. Iodid was found in the contents of the bullæ and in the urine. The case is mentioned as an unusual form of an eruption produced by potassium iodid in an extremely susceptible patient.

Dr. F. C. Knowles, Philadelphia: In reference to the possibility of an eruption being produced by small doses of potassium iodid, I would refer to the case of Mackenzie, who described a case in an infant of five months where a small dose produced an eruption in 45 minutes, and the child died ten hours later.

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PEMPHIGUS FOLIACEUS

WITH REPORT OF A CASE

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OMAHA

Pemphigus is a skin disease characterized by the eruption of blebs. These are, however, not characteristic in themselves but only in connection with other important features. The whole subject is not sufficiently cleared up yet and there is no unanimity as to what to include and what to exclude. Dermatitis herpetiformis is still considered pemphigus in Germany. Various skin diseases are denominated pemphigus, such as pemphigus neonatorum, which most probably is a bullous form of impetigo contagiosa, pemphigus syphiliticus, a manifestation of syphilis, pemphigus neuroticus and hystericus, sequels of functional and organic nerve disorders. A strict avoidance of these names would clear the ground rapidly. Bullæ are seen in bullous dermatitis, bullous erythema, and bullous urticaria, but nobody thinks of including these in pemphigus. Whether there is an acute pemphigus is a matter of controversy and denied by many.

What then does constitute real pemphigus? In the first place the characteristic feature is the bleb, which must be elementary, that is must begin as such and not be due to secondary changes of other skin lesions. It must be the essential and not an incidental or unusual feature of the disease. It must not be a local condition but the manifestation of a grave internal disorder. Its course is chronic, with exacerba-

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tions and remissions, leading to a deep systemic depression and frequently to death. With such restrictions it may easily be seen that many cases of pemphigus reported must be excluded from consideration under this head and that pemphigus as an idiopathic disease (called so in the absence of a better knowledge of its nature) is a rare disease.

Of the etiology of pemphigus nothing is known. Against a microbic theory speaks the fact that the contents of fresh bullæ are sterile; that there is no clinical evidence of its contagiousness; that not more than one case in one family has been reported. A toxic process was considered from the analogy of the action of certain poisons and drugs which, when introduced into the system, were followed by the eruption of blebs. The occasional increased percentage of eosinophils was used for this argument. Many attribute pemphigus to a neuropathic cause, arguing that some functional and organic nerve disturbances manifest themselves by the appearance of blebs. Numerous examinations of peripheral and central nerve tissues in autopsies have shown no pathological changes in them. Age, sex, race and climate have no predisposing influence. Riecke says very tersely, that our total ignorance of the etiology of pemphigus serves as a valuable diagnostic point in its differentiation from other bullous diseases.

Of the three varieties, pemphigus vulgaris, foliaceus and vegetans, the last two are the rarest. Pemphigus foliaceus, of which I wish to report a case, is clinically so different from pemphigus vulgaris that it might be considered a separate disease, were it not for the fact that they sometimes lapse into each other. Pemphigus foliaceus occurs only once in 5,000 skin diseases and Croker has only seen six cases in a life-time of extensive dermatologic practice. Pemphigus foliaceus is a chronic disease which breaks out in successive crops, until it finally involves the whole surface. The cutaneous lesions are flaccid bullæ containing only sufficient fluid to bag

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their dependent parts. The contents are cloudy almost from the first and soon become purulent. The blebs rupture quickly and the epidermis exfoliates in shreds leaving the corium denuded and moist. The raw patches are covered with a foul-smelling sero-pus and have no tendency to dry up and to be covered with a healthy epidermis. The exudation undermines the neighboring skin, giving it a shriveled appearance and looks, as Cazenave says, like a flaky pie-crust. When the disease is fully developed, the body is covered with raw areas of various size, shreds of epidermis and loosened skin.

The mucous membranes may take part in the process, a complication considered especially unfavorable. The general health may not suffer at first, but the patient becomes ultimately cachectic or dies from an intercurrent disease. The end is almost always fatal, though sometimes not until after a few years.

The pathology of pemphigus has been thoroughly studied. The location of the bleb may be interepithelial or between the epidermis and the corium. The epithelial cells are edematous and swollen. The interspinous spaces are occluded. The corium is the seat of a mild probably secondary, inflammation. The papillary blood-vessels are dilated and surrounded by small mononuclear leucocytes. An excess of eosinophils is found occasionally in the blood and the serum and was for a time considered distinctive, but no special significance can be attributed to it. In autopsies of bodies of persons dead from pemphigus, only coincidental changes were found, but nothing directly pertaining to the disease.

REPORT OF CASE

On March 15, this year, I first saw F. A. S., a farmer, 36 years old. Father died at the age of 60 of pneumonia, mother at 59 of typhoid. Seven brothers and one sister are living and in good health. There is no knowledge of a similar disease in the family. The patient has always been in good health outside of the usual children's diseases. His present trouble began in September, 1909, as small clear vesicles in the mouth, which

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increased in size and spread to the throat. Two weeks later they appeared in different places over the entire body. At first they remained unbroken and dried up, leaving behind considerable pigmentation which can still be seen. The disease was at that time probably pemphigus vulgaris. Lately the character of the bullæ has changed; they do not last long enough to become filled and tense, are only partially filled and flaccid and rupture rapidly. Large raw patches are produced in this way, partly covered with a sticky serum, partly with shreds of the exfoliated epidermis. The whole body is affected with the exception of the face, especially the lower third of the legs and the buttocks. Between the excoriated areas the skin shows plainly the separation of the horny layer from the subjacent layers by the above-mentioned shriveled finely wrinkled appearance. An exceptional feature, which I find observed only by Weidenfeld[1] was also seen in this patient. A slight rubbing of the skin or a mild trauma, like the taking of a drop of blood from the ear-lobe, was invariably followed by a large bleb. This is probably not so much due to an unstable condition of the vasomotor system of the skin, as in epidermolysis bullosa, as rather to the unstable adhesion of the individual layers of the epidermis. The mucous membranes were affected from the first. The tongue, gums, cheeks and the pharynx are involved presenting sharply outlined raw patches, partly bleeding, partly covered with a loosened grayish membrane. The eruption was at first accompanied by itching which has subsided lately and only general discomfort is complained of. Chewing and swallowing is at times extremely painful and almost impossible. The general health has not suffered much up to the present time, except for an occasional rise of the temperature and an anemic appearance. The patient has, however, lost 70 pounds in his weight since the beginning of his trouble. The urine is acid, specific gravity 1011; no albumin or sugar is present. Blood examination is as follows: Red cells, 4,232,000; white cells, 6,600; hemoglobin, 82 per cent. Differential count: Small mononuclears 40, 20 per cent.; large mononuclears, none; transitional forms 28, 14 per cent.; polymorphonuclears 128, 64 per cent.; eosinophils 4, 2 per cent. As can be seen from this, there is no considerable change from the normal except a decrease of hemoglobin. The percentage of eosinophils is not increased.

400 Bee Building.

1. Cited by E. Spiegler: Mraczek's Handbuch der Hautkrankheiten, II, 2.

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Pemphigus foliaceus.

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ABSTRACT OF DISCUSSION

DR. M. MCMAHON, Palmyra, Ill.: I have under observation a case of pemphigus, in an anemic woman, 55 years old, who has worked hard all her life and is broken down in health. The first lesions appeared about six months ago on the buccal mucous membrane, and finally covered the entire buccal mucous membrane, including the gums. After a time, the patient's condition improved to such an extent that she could take food, which she was unable to do at first. Early in March, the first external manifestations of the disease appeared on the face. Other regions of the body then became involved, many blebs forming and breaking down, leaving large areas of denuded skin. Then for a time the patient would improve, only to go through the entire process again with a fresh crop of lesions. Another physician saw the case with me, and confirmed the diagnosis. At the present time, the external manifestations of the disease have somewhat improved, but all the mucous membranes, including the throat, stomach and intestines are now undergoing the same process. The urine, which has been repeatedly examined, contains neither sugar nor albumin, but does contain a large amount of indican. The patient has had all sorts of treatment, arsenic, salicin and quinin being the principal internal remedies, although she had an idiosyncrasy against the latter drug. She appears to be improving at present, but on account of the condition of the mucous membranes, she cannot take a great amount of nourishment. This is the only case that I have seen in the section of Illinois in which I live. I recall a case in the City Hospital about twenty-eight years ago in which the patient was kept in a continuous bath for about six months and finally died.

DR. H. H. HAZEN, Washington, D. C.: I reported a case of pemphigus foliaceus in the *Journal of Cutaneous Diseases*, March, 1910. The patient was a man, 30 years old, who first came under my observation in 1907, and who was referred to me for study by Dr. Thomas C. Gilchrist of the Johns Hopkins Hospital. In going over the metabolism of this case, we found the ammonia output tremendously high. Normally, the ammonia is but 3.5 per cent. to 5 per cent. of the total urinary nitrogen, but in our case the ammonia constituted 15 per cent. of the total urinary nitrogen. This spoke in favor of intestinal infection. The patient was treated with autogenous vaccines in doses ranging from 10,000,000 to 100,000,000. After the first injection he became ill, with marked malaise and headache, pain in the back and limbs, redness and swelling at the site of the inoculation, and an outbreak of a fresh group of vesicles. The reaction was similar to the typical tuberculin reaction. As each injection caused more blisters and malaise, the treatment was stopped. In view of Crowe's work, large doses of hexamethylenamin were given, but without effect.

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The patient was placed in a continuous bath during the day; at night he slept in bed. After a few days it was noted that the scales had decreased in number, but there was a large number of fresh vesicles which were moist and flaccid. The patient's general condition, however, had improved. He did better under this treatment than any other.

I think that there is need of more thorough investigation of the entire group of pemphigoid eruptions along the lines of modern research. It is not sufficient merely to employ observation. Studies should be made on the following subjects: (1) general metabolism; (2) toxicity of the perspiration; (3) bacteriologic examinations of the blood, bullæ, urine and feces; (4) agglutinating power of the blood.

DR. E. S. LAIN, Oklahoma City: Has any one experimented with the *x*-ray in these cases? I have had the opportunity of making such a test in two cases during the past twelve months, and under this treatment it has seemed to me that the exacerbations terminate much more rapidly than by any other method that I have tried. In my first case, the lesions ceased to form after the eleventh exposure to the rays. Since then the patient has not been directly under my care, but the lesions have been so few in number that her attending physician did not think it necessary to bring her to the hospital for further treatment. Of course, I do not regard the patient as cured.

In another case, which I saw a month later, the blebs ceased forming after eight exposures to the *x*-rays. Four weeks later there was a recurrence, but thus far the patient has failed to return to the hospital for further treatment. I have a photograph of this patient which I will show to-morrow at the photographic exhibit.

DR. A. SCHALEK, Omaha, Neb.: Dr. Hazen's remark that cases of pemphigus foliaceus have not been studied in a sufficiently thorough manner is not quite justified. The disease is so rare and interesting, especially on account of its serious consequences, that any one who ever had a case generally took the time to study it. In spite of that fact, we do not know much more about the etiology of the disease than we did before. I have watched my cases carefully, and I have had blood examinations and cultures made.

In my paper, I did not say much about the treatment of pemphigus foliaceus. So far as I know, there is no satisfactory treatment; the patients all die, some sooner, some later. I put my patients in a warm bath for several hours every day, and then have them wrapped in moistened sheets.

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DERMATITIS EXFOLIATIVA

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The name "dermatitis exfoliativa" may be given to any inflammatory disease of the skin which has for its most prominent features, inflammation and exfoliation of the epidermis. There may be features, however, histologic, etiologic or otherwise, which can be used to advantage in designating some of the types. Brocq recognizes seven types of exfoliative dermatitis. It may not be necessary to make as many distinct divisions as this, since several of these types may have the same or similar etiologic factors and differ only in degree of severity; still, we must acknowledge that there are as many clinical types as he describes.

The case I am about to report is evidently related to the more frequently seen cases of erythema scarlatiniform. Still I think that it would be a mistake to consider them identical.

The type known as "dermatitis exfoliativa neonatorum" or Ritter's disease, is a distinct type, and is generally conceded to be due to an infection at or near the time of birth.

The distinct type described by Hebra as "pityriasis rubra" is generally considered a fatal disease, but from time to time we have reports of recoveries of cases in all respects resembling this type, with the exception that they recover. There seems to me no adequate reason why they should be put in a different class. Frank Woodbury,[1] reports two cases, which he considers

1. THE JOURNAL A. M. A., 1899, xii, 81.

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identical as examples of this disease. One of the patients died and the other recovered.

We have many other diseases which tend to a fatal termination in the severe cases, but in the milder cases of the same kind the patients recover. Why should we not consider this disease capable of the same variation and conclude that, while many patients die, others recover?

REPORT OF CASE

Patient.—B. K., a girl, 8½ years old at the time of first appearance of this skin disease, in April, 1907; her family history was negative. Her father, mother and two sisters are healthy. The cutaneous history of the family is negative. The patient had been healthy up to the time this disease made its appearance. Her skin was fair, hair inclined slightly to red, temperament nervous in mild degree, rather slender and of medium height for her age. She lived with her parents on a farm, where sanitary conditions are supposed to be good.

Present Illness.—The disease made its appearance as spots of reddened, rough skin, inclined to scale. These spots ranged from the size of a split pea to that of a silver dime; some were circular, while others were irregular in shape. The distribution was general over the body and extremities. At one or two places several of these lesions coalesced, forming irregular patches. Desquamation was in small scales. There must have been decided itching, as the parents say the child scratched until the blood flowed. Even while asleep, she scratched, which is indicative of severe itching. Her appetite was irregular and health not up to par. The parents of the child supposed this to be a case of multiple ringworm of the body, and it was treated as such. No physician was called at that time. In August, 1907, she had typhoid fever. This ran a reasonably mild course, the temperature at its highest being about 103 F. While the fever was present the skin disease disappeared completely, just as we see sometimes in psoriasis. When she recovered from the typhoid fever about September 15 the skin lesions returned, apparently about as they were before the typhoid made its appearance. They were the same red, slightly scaling spots as at first. The lesions were more numerous on the thighs than in other localities, but they were quite general in their distribution. This condition continued all through the winter, and in the spring of 1908 the family physician was called in to see the case. He considered it a case of

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disseminated ringworm and treated it accordingly for the next six months. There was no permanent improvement, but an increase in size of the lesions with more scale formation.

Examination.—When I first saw the case, Nov. 20, 1908, there were only a few of the smaller scale lesions present, and these were scattered about over the trunk and extremities without definite grouping. The larger ones had grown in size, ranging from 1½ to 3 inches in diameter, and were circular or oval in outline, not noticeably elevated above the surrounding skin, and had an erythematous base with thin papery scales covering the surface. At two or three places, several of these lesions had coalesced and formed irregular patches, but most of them were still discrete and were scattered promiscuously with the thickest distribution on the thighs. The distribution was about equal over the flexor and extensor surfaces. The lesions were sharply marginate.

Course of Disease.—My first impression was that I had an atypical psoriasis to deal with. An ointment was given, containing small quantities of salicylic acid and resorcin, in addition to internal treatment, and the patient was requested to return three weeks later. Promptly in three weeks the patient was brought to see me again. The change in these three weeks was great. Instead of scattering lesions, the entire skin was involved. I was informed that this involvement came, not by formation of new patches, but by extension of those present before. The whole process took on a more active appearance; the skin became brighter red and somewhat thickened. The process was extending up over the face and scalp, where it had not appeared before. The worst of the inflammation, however, all through the disease, was on the thighs and trunk. The face and scalp suffered least. This extension was accompanied by chilly sensations and fever. This begun about December 1. The temperature was usually not high, but for the next two months it seemed to be always somewhat elevated, ranging from 99 to 103. There was no particular time for the increase in temperature, but the high points were just as likely to be in the early morning as late in the day. The discomfort of the patient, due to chilling, was quite marked, especially when circulating air came in contact with the denuded surfaces. Desquamation soon followed the extension of the inflammation. This desquamation left large patches of raw, oozing, sensitive skin. This was so general that the underclothes became at times saturated with the serous fluid. The patient did not complain of itching, but of a burning sensation, which she tried to relieve by rubbing. Desquamation

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occurred in small scales over the body and extremities. The palms and soles desquamated in large pieces. Toward the end of the disease the nails from the small toe on both feet desquamated also. The other nails were rendered rough and ridged, but remained intact. The urine was examined at several different times and nothing abnormal was found. The heart, lungs, liver, spleen and all other abdominal and pelvic organs were normal as far as could be ascertained. No blood-count was made. The inflammatory process subsided gradually, the oozing grew less by degrees until it ceased altogether, the desquamation gradually disappeared along with the erythema and the skin became normal in appearance again. This point was reached about the end of April, 1909, about five and one-half months after I first saw the case. During the course of the disease the child had lost flesh until the bones became prominent. Now her appetite returned and the lost flesh was regained and more. A year from full recovery of this patient she remained perfectly well, has grown normally and has a skin as perfect as any child. In fact, there is no trace of the old trouble.

Treatment.—This consisted, first, of the application of soothing applications to relieve the disagreeable sensations; oily preparations seemed quite effective and agreeable to the patient; second, of tonic remedies internally. Various tonic remedies were used, as seemed indicated. Along with this I tried the efficacy of quinin. I realized that this case was different from those in which Mook[2] seemed to secure so much benefit, but gave it a trial. The benefit received from this treatment was not great, but nevertheless the child's parents claimed some improvement from it. I could not say that treatment accomplished anything in a specific way; it merely supported the patient's strength and palliated the suffering, while Nature produced a cure.

I do not believe that the causative factor in all cases of this type is the same. As in scarlatiniform erythema, which it resembles, the causes may be various. In the case just reported I thought at first that the general inflammation might be due to the local application of resorcin or salicylic acid. It is true that these were applied in mild strength and would have required a skin with an idiosyncrasy to have produced the inflammation.

2. Jour. Cutan. Dis., xxvi, 408.

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The involvement of the entire skin, even where none of the ointment was used, made it apparent that this was not the cause. Also we see that the inflammation continued and grew worse after the local applications were withdrawn. The continuation of the inflammatory process for three months before beginning to abate would indicate the continuation of the cause for that length of time. That this cause was a toxic agent generated within the body I believe to be the rational explanation of the trouble.

ABSTRACT OF DISCUSSION

DR. FRANK C. KNOWLES, Philadelphia: In the *Journal for Cutaneous Diseases* for January, 1910, Dr. John T. Bowen, of Boston, published a paper in which he described seven cases of dermatitis exfoliativa, five ending fatally. In a previous paper, presented to the American Dermatological Association in 1902, he divided these cases into four types. The first was the recurrent desquamative scarlatiniform dermatitis; this form might occur after the ingestion of drugs. The second was the dermatitis exfoliativa of Wilson; the third occurred as a sequel to psoriasis, eczema, lichen planus, etc., and followed the administration of certain drugs, such as belladonna, mercury and quinin; and the fourth form was the pityriasis rubra of Hebra. I have seen a few cases of dermatitis exfoliativa, and recently, since the first of the year, I have seen a generalized case which followed the administration of quinin, and another in which the eruption appeared following the local use of a mercurial ointment. In this case the application was followed by an immediate generalized exfoliation of the skin.

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ANOMALOUS SCARLET FEVER

A REPORT OF THREE EPIDEMICS

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During the past decade there have occurred in Lakeside Hospital three epidemics of what is thought to be anomalous scarlet fever. In each of these epidemics the disease might have passed unrecognized or at least some doubt might have been entertained as to its nature, had not one or more typical cases occurred which acted as a diagnostic control. These epidemics were characterized by the mildness of the attack, the benign course of the disease together with the suppression or complete absence of the exanthem together with some other of the more important symptoms.

The first epidemic occurred in the winter of 1904-5 and started in the children's ward, but before strict quarantine and disinfection terminated its spread, the medical and surgical wards likewise contributed until eighteen cases were observed.

REPORTS OF CASES

CASE 1.—A child admitted with some slight ailment was observed to have a faint rash on the neck and face which soon disappeared, although a redness of the fauces persisted somewhat longer. There had been but a slight rise in temperature and the case attracted no special attention.

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CASE 2.—A child aged 3 was admitted to the surgical service with tuberculosis of the knee. On November 30 the knee was aspirated and iodoform emulsion was injected. December 1 the temperature, which had been about normal, registered 103 F.; it became normal again on the 2d, and the following day again arose to 103. On the 4th a slight reddish, papular rash noticed over the trunk with flushing of the face. This was thought to be due to iodoform poisoning. Further examination, however, brought to light changes in the fauces; and the tonsils were red and slightly swollen. Three days later, December 7, the night nurse on duty in this ward came down with a typical infection of scarlet fever of moderate severity, whereon both were immediately isolated. The child ran a mild course with slight desquamation and was discharged Jan. 13, 1905.

CASE 3.—The case of the nurse above mentioned ran a typical course of moderate severity. It is noted that differential blood-count showed a marked increase in eosinophils.

CASE 4.—A child, aged 11 months, was in the surgical service for a hare-lip operation. Some time after the operation it was noticed that the temperature, which had been normal, suddenly arose to 103 but returned again to the normal two days later. Three days after this, December 4, it registered 101 and the next day the face was flushed, except around the mouth, and a slight rash could be made out over the body. There was also inflammation of the throat. The child was isolated, and three days later the rash had disappeared. The temperature at this time was 99. Desquamation had already begun around the neck. From this time the temperature became irregular and later a discharge was noticed from the left ear. The notes of the case show that the child was discharged well, Jan. 11, 1905.

CASE 5.—A hospital nurse, aged 19, complained of a headache, was chilly with a sore throat on December 4. On the afternoon of the same day the left tonsil was red and puffy with pin-point white spots. The temperature was 101.6. The next morning she still had headache and vomited once after taking magnesium sulphate. The tonsil being still "puffy and sore" the patient was taken to the operating-room to have it incised when one of us was asked to see the case. A diagnosis of scarlet fever was made and the patient isolated. Previous to this no rash had been seen although a slight itchiness of the skin had been complained of. At the time of our examination, however, a pinkish velvety rash could be made out on the sides of the neck and upper part of the chest. The face was deeply flushed, except about the mouth. The following day the rash

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was well out and of typical appearance. It then became patchy and began to fade two days later. Both tonsils became covered with a grayish exudate and general glandular enlargement was present. Throat cultures showed the staphylococcus and streptococcus. Blood count on December 4 showed eosinophilia 8 per cent.; no other change noted. The case thenceforth ran an uneventful course.

CASE 6.—A hospital nurse, aged 29, on December 8, complained of chills, sore throat, headache and vomiting. These, however, were not very severe and she continued on duty. Her appetite seemed unimpaired. Two days later the face, shoulders and outer aspect of arms were found to be flushed. The tonsils were slightly enlarged and injected and the tongue coated. The following day the erythema had assumed a blotchy appearance and was limited to the regions first involved. It did not extend and was followed by a slight branny desquamation on the arms and face. During the whole course the temperature did not go above 99.

CASE 7.—A child, aged 4, was admitted to the hospital December 6 suffering from acute bronchitis; while in the ward the temperature ran from 99 to 100. On December 21 the child had a slight erythema on the trunk, legs and face and the tonsils were red and swollen. The next morning the rash was faint, the tongue was coated and the tonsils were very large. By the 25th the rash had disappeared; although the patient was under close observation no appreciable desquamation followed. The urine showed a faint trace of albumin from December 12 to December 24. The temperature was never above 100.

CASE 8.—The patient, a child aged 3, on surgical service was operated on for club-foot on December 6, and on the 7th the temperature arose to 100.5 and remained between that point and normal until December 14. On that day, although the patient had not formerly complained, the temperature arose to 102.5 and there was a slight reddish punctate eruption over the body with the face flushed, excepting the circumoral region. The tongue later presented a strawberry appearance and the tonsils were large and red. There was a general glandular enlargement. On the 20th desquamation began and the child was discharged well one month later.

CASE 9.—A nurse, on duty in the infected ward, had scarlatina accompanied by arthritis, which was not severe. Her case ran a typical course. The patient made an uneventful recovery.

CASE 10.—A laborer, aged 30, was admitted to the surgical service for a herniotomy. On December 20, four days after

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admission, there was a slight rash on the body with an injected throat and large, red tonsils. The tongue was swollen and coated, glands enlarged. On January 1, desquamation started and patient was discharged January 16. At no time was the temperature above normal excepting on December 29, when the wound became infected and the temperature remained above normal for a few days. The leucocyte count was 23,000, eosinphiles 11 per cent., blood-cultures negative.

CASE 11.—A miner, aged 28, had been admitted to the hospital on September 4 for paraffin injection of the nose. On December 22 the patient had swollen tonsils, a suggestive tongue and a very slight, pinkish, macular rash on the body, the macules being from ⅛ to ½ an inch in diameter with a slight erythema between them and looking somewhat like measles. There was no enanthem on the buccal mucosa, no nausea, sore throat or fever; but the patient had some headache and general glandular enlargement. On December 21 there was a slight desquamation on the right hip which lasted only a few days; no desquamation was noticed elsewhere. The urine showed a faint trace of albumin from December 23 to January 10; the temperature was never above 99.

CASE 12.—The patient, a nurse aged 20, on December 14 had some headache, sore throat and felt feverish, vomiting four times. On examination there was a slight erythema of the arms, over the region of the scapulæ and on the face, except the circumoral region. The patient also had a coated tongue and swollen, red tonsils covered with a slight exudate. The glands were not enlarged. By the 20th the rash on face and arms had faded, having appeared nowhere else, and on December 28, there was a very slight desquamation present on the areas involved. The nurse was discharged January 9, having never had a temperature above 100 and that only during the first night. The urine showed a faint trace of albumin up to January 6.

CASE 13.—A nurse, aged 23, on December 15 had headache, sore throat, and felt chilly and feverish. The next day there was a slight rash on the chest and neck with a temperature of 100.5. The tongue was swollen and coated, and the tonsils red and enlarged. The glands about the neck showed enlargement. By the 20th the rash had disappeared but no desquamation followed. On the 24th the throat again became sore and the glands enlarged and tender with a rash over the whole body. Then typical desquamation appeared, and the patient was discharged January 10. Except during the first night the temper-

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ature was never above 100. The urine showed a faint trace of albumin for a few days.

CASE 14.—A maid employed in the hospital, aged 25, on December 22 had a sore throat, headache, backache and was nauseated. She continued to work until two days later, when on examination she showed a flushed face, except the circumoral region, with erythema over the chest and shoulders. The tongue was large and coated, papillæ prominent, tonsils red and swollen and glands generally enlarged. The erythema was entirely gone by December 27, but the patient never had the slightest trace of desquamation. The urine showed a faint trace of albumin from December 25 to the 29. There were no casts. The leucocyte count was 13,600, eosinophiles 13 per cent., throat cultures gave staphylococci and streptococci. The temperature was never above 99 nor was the pulse over 100.

The remaining cases in this epidemic showed nothing unusual except that they were very mild and comparatively of short duration. The points mainly to be noted in this epidemic are the following:

1. The relatively large numbers of adults, chiefly nurses in the infected wards. Of eighteen attacked, eight were adults, six were nurses or otherwise employed in the wards, and two were adult patients exposed while in the wards.

2. The benign character of the infection and its short course, (average being 3.9 weeks from appearances of rash to end of desquamation). The only constant symptoms that could be regarded as at all typical were the onset and the congestion of the fauces. The cutaneous manifestations, with two exceptions, are evanescent and alone insufficient for the purpose of diagnosis.

The second epidemic began in April, 1907; there were eleven cases reported, although the case notes were found even less complete than in the first epidemic. As nearly as can be ascertained the epidemic began in the children's ward as an indefinite sore throat with no distinct or constant cutaneous manifestations.

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Convalescence, however, was more protracted than was observed in the first epidemic and even a larger proportion of adults were attacked. The following may be taken as the most typical examples of this epidemic.

CASE 15.—A nurse, aged 20, was admitted to the isolation pavilion April 19, 1907, after having had a slight sore throat, headache and malaise since April 16. On examination there was a faint rash over the entire body, general glandular enlargement, tongue negative, tonsils injected and the right one enlarged. There was nothing abnormal in the heart or lungs. The rash disappeared by April 22 and desquamation, which was never very profuse, did not start until May 1 and lasting until July. The temperature was never above 99.5, excepting at one time, when it went up to 100.3. The pulse was never more than 110; urine was negative. The patient was discharged July 1, 1907.

CASE 16.—A nurse, aged 21, on July 13 complained of sore throat, weakness, nausea, cold perspiration and fever. The next day she noticed an eruption and on examination there was found a marked erythema with edema of the face. There was a strawberry tongue, throat swollen, tonsils covered with a membrane, glands all palpable. The cutaneous rash and the membrane in the throat were gone by May 18 and desquamation started lasting until July. The temperature on admittance was 104 and pulse 120, both of which came down to normal in four days. No complications were noted, excepting a slight trace of albumin in the urine. Cultures of the streptococcus were obtained from the throat.

CASE 17.—A nurse, aged 20, with previous history of rheumatism and chorea, had been on duty in the infected ward. On May 9 she complained of weakness, sore throat and malaise. On the 10th a rash was noted on the chest, arms and neck and on examination there was a faint erythema over the entire body, with a strawberry tongue, swollen tonsils covered with a heavy membrane and general glandular enlargement. The throat swab showed only streptococcus. The rash was gone by the 13th and desquamation began about a week later, being finished by July. The patient developed a slight arthritis and myocarditis. The temperature remained about 101 until the 15th. The urine showed a faint trace of albumin.

CASE 18.—A nurse, aged 19, awoke on May 9 with a slight sore throat, nausea, malaise and slight fever. The next day a

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rash was noticed and on examination the patient had a very slight erythema over the entire body with a negative tongue and injected throat and tonsils. The superficial glands were slightly enlarged. Desquamation began on the 25th, lasting until July, although never very extensive. The urine showed a faint trace of albumin; there were never any casts. The temperature was 100 on the first day, after that normal.

CASE 19.—A nurse, aged 20, on May 4 complained of severe sore throat, nausea and malaise. Early in the afternoon an eruption first appeared on chest and neck. The following day a general marked erythema was present with glandular enlargement, tongue large, swollen, reddened, and throat greatly congested. The rash had disappeared on the 19th, and the throat was normal by the 21st. Desquamation began June 1 and lasted until July 17, although never very profuse. The temperature on admission was 102, but soon fell to normal where it remained. The urine showed a faint trace of albumin.

In this epidemic, as in the one preceding, there developed no serious complications or fatal results. The features to be noted are the sudden onset with marked involvement of the fauces and comparatively high temperature followed by a varying degree of the exanthem. There was a rapid subsidence of all symptoms followed by a retarded but protracted period of desquamation.

What may be termed the third epidemic occurred in 1909. Although but three cases were observed they furnished features that are thought worthy of mention.

CASE 20.—A child, aged 9 months, was on the surgical service for cervical adenitis, being admitted Oct. 31, 1909. It had some discharging sinuses which were being packed with iodoform gauze, and on March 21 the child developed a slight scarlatiniform rash with a temperature of 100. The rash was faint, atypical, lasting only three days. There was no nausea or vomiting. The throat was congested and reddened, while the tonsils were enlarged. At first the case was regarded as an iodoform rash, but as the patient had 7 per cent. of eosinophiles in a differential count of 200 cells she was isolated, and while in isolation had a typical desquamation and double otitis. The urine also had a faint trace of albumin. The temperature never went above 100 until the otitis developed.

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CASE 21.—The child in the next bed to the patient last described came down three days later with a typical scarlet fever. She was a girl aged 3, in the hospital for acute anterior poliomyelitis. The rash was marked and typical, with a temperature of 103, rapid pulse, vomiting, severe sore throat and a considerable enlargement of the tonsils. Two days later the rash faded and the case ran a typical course of desquamation with eventually a complete recovery.

CASE 22.—A nurse, aged 24, was nursing the child with obscure so-called iodoform rash. Two days later she was taken off duty because of a sore throat and a feeling of malaise and headache. The throat was very red and edematous, the tonsils greatly swollen so that they met in the median line. They were partially covered with a membrane but showing no diphtheria bacilli. The glands were not enlarged, except those of the neck. The temperature was 100 on admittance, 103 two days later and afterwards never above 100. On December 1 the patient vomited several times but the tongue was never typical. The leucocyte count was 19,000; differential showed no eosinophilia; urine was negative. The patient never showed any rash or desquamation, but considering her symptoms it was deemed justifiable to place her in this list.

CHARACTERISTIC FEATURES

The most striking characteristics in this series of 32 cases occurring in three epidemics were the following:

1. *Erythema.*—There were three cases in which erythema was very slight; in one it was absent and in one it was confined to small areas and very evanescent. Two of the patients with slight erythema had it confined to the neck, shoulders and arms. It may be well to mention, in passing, that one patient had a secondary erythema.

2. *Temperature.*—This varied from normal to 105 F. Four patients never had a temperature above 99, two never above 100, and the remainder ran between 100 and 105, most of them, however, between 100 and 102.

3. *Desquamation.*—There were six cases in which the desquamation was typical and one in which it was faint but general. One patient never showed any desquamation except around the neck; another none ex-

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cept on the right hip. There were two in whom it was confined to the face, arms and shoulders and three never showed any desquamation.

4. *Urine.*—In only two cases was there absence of all signs of nephritis, while all the others had a faint trace of albumin; and in one case, there were casts. Two of the three patients showing no desquamation had a faint trace of albumin for a few days.

5. *Angina.*—Practically every patient in this series had a severe angina, seven of them also showing presence, more or less, of a membrane in the throat.

6. *Blood.*—The only changes noted were a marked increase in the number of leucocytes in a few cases, and in a number of instances the differential blood count showed a high percentage of eosinophiles, which is in accord with the observations of Van den Berg[1] and Kotschetkoff.[2]

LITERATURE OF THE SUBJECT

In the literature dealing with this special phase of scarlet fever, namely, the absence of exanthem with little or no rise of temperature together with other manifestations characteristic of a faint type of the disease, we find as far back as 1839, Taupin[3] observed, during the course of his internship at the Hôpital des Enfants Malades, an epidemic of five cases of scarlet fever in two of which there was no eruption. The year previously Eiselt[4] published an account of a severe case of scarlet fever in a girl of 20, in which there was no eruption, although the girl had a marked desquamation associated with anasarca. She eventually recovered.

Buttura[5] in 1857, was called on July 10, 1856, to see a young man who suffered from a well-marked scarla-

1. Van den Berg, J. B.: Arch. f. Kinderh., 1898, xxv, 321.
2. Cabot, R. C.: Clinical Examination of the Blood, New York, 1897, p. 177.
3. Taupin, Charles: Essai sur la scarlatine sans exanthème, Thèse, Paris, 1839; abstr. in Jour. conn. méd.-chir., vii, 151-155.
4. Eiselt, J. N.: Fall einer Febris scarlatinosa sine Exanthemate, Med. Jahrb. d. k. k. oesterr. Staates, Wien, 1838, New Series, xv, 212.
5. Buttura, C. A.: Des fièvres éruptives sans éruption et particulièrement de la scarlatine sans exanthème, 1857, Paris.

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tinous angina. The eruption was copious and the disease followed a course typical of scarlet fever. Four days later a little girl in the same family developed croup; angina marked but no eruption throughout the course of the disease. Five days later on June 20 a little brother also developed intense characteristic anginous symptoms; the odor from the mouth was pronounced. No eruption could be observed at any time. Convalescence was prompt in all three. There were no sequelæ.

Buttura then enters into a discussion concerning the opinions of authors in regard to the possibility of scarlatina without eruption, and reviewed the literature of this subject at some length. He states that in September, 1829, there reigned in the village of Seine-et-Oise an epidemic of so-called common angina. Careful study by the local physician led to a diagnosis of scarlet fever with predominant mouth (throat) symptoms. In the Château de Villeroy, inhabited by Comte Friant and his family, thirteen persons were affected, and of these, five presented a special angina without eruption.

Trousseau observed scarlatinous angina without eruption of the skin in 1828, at Cour-Cheverny. The diagnosis was made on the strength that a boy had distinct scarlet fever with eruption. Three sisters of the boy developed fever, angina, but no eruption.

He states that Dr. Carrière observed during an epidemic at Saint-Dié (Vosges) during the winter of 1842-1843, 34 cases of scarlet fever with an eruption in 23 only, and in the majority of these it was very slight. The disease ran a benign course. In one case of scarlatinous edema with albumin in the urine; no sign of eruption appeared, although all the other symptoms of scarlet fever with angina were present.

Bouché (of Vitray) reported four cases of scarlet fever as follows: The first was typical scarlet fever without eruption; the next a typical case with eruption;

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the third was again without an eruption and the fourth again a usual case. Two of the cases were without eruption. The diagnosis was made from general symptoms and the presence of eruption in the other two cases occurring in the same house.

Legroux reported a case of scarlet fever in a chlorotic woman in whom the eruption could barely be made out. The eruption was likewise scarcely perceptible in an infant of four days who is supposed to have contracted it from the mother, who had scarlet fever on the second day of puerperium. The father had an angina without fever or redness of the skin at the time that the scarlet fever terminated in the mother.

In another house a boy had ordinary scarlatina; the sister developed a marked angina, with pronounced scarlet eruption and died. During the course of this affection the mother, her infant, and a young woman of 24 contracted angina with pseudomembranous plaques, with fever, but without eruption, lasting six days. Three days after the death of the child, the grandmother and the father presented guttural angina, slight fever, characterized by a bright redness, but no swelling.

During an epidemic in Berlin, Dr. Helft observed cases in which no eruption appeared although all the other symptoms prevailed, occurring in families in which scarlet fever was present.

In an epidemic of scarlet fever at Loudon (Vienne) from March to September, 1841, Mondière reported that in one case of very severe angina the eruption was confined to the feet and hands only. In other cases no eruption appeared.

During the epidemic at Loches, 1835, Renaud observed three cases of scarlet fever in one family. Two children developed typical cases of the disease when the third one was stricken with all the severe symptoms that the others had shown, but at no time during the attack did it develop the slightest sign of an erup-

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tion. The course of the disease was quite severe in this case, but the child recovered.

Berrand further states that Krauss of Tübingen reports having observed scarlet fever without eruption in the proportions of 1 in 3. The cerebral symptoms predominated in these cases. He states that Dr. Maclintock reported three cases as follows: Child was taken with vomiting; condition did not improve; coma alternating with spasms, death ensued. On the day this child was buried another in the family was taken in the same manner; developed the same symptoms; marked convulsions and death. The third child was also taken. It, however, developed a typical scarlatina rash. No doubt the other two children died from scarlatina without exanthemata.

About the time Buttura's article appeared Bauer[6] reported an epidemic of 20 cases, among them being that of a boy who had, he thought, a very severe scarlatina, yet developed no observable eruption at any time. The patient eventually recovered after having had a post-scarlatinal arthritis.

Anderson,[7] Banks,[8] Whelan,[9] Robinson,[10] Dreyfus,[11] and Brissoe and Wetherill,[12] also reported similar cases about this time, all agreeing that in their experience scarlatina at times existed with absence or sparseness of the eruption as well as other symptoms of scarlatina. At such times it is impossible to make a diagnosis were it not for the fact that an epidemic of scarlet fever is in progress.

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6. Bauer, F.: Beitrag zum anomalen Verlauf des Scharlachfiebers, Ztschr. f. med. Chir. u. Geburtsh., 1859, xiii, 97.
7. Anderson, W. J.: Some Anomalous Cases of Scarlatina, Lancet, London, 1854, i, 327.
8. Banks, J. T.: Dublin Hosp. Gaz., Anomalous Scarlatina, 1858, New Series, v, 65.
9. Whelan, J. H.: Modified and Anomalous Scarlatina, Lancet, London, 1883, ii, 769.
10. Robinson, C. H.: Scarlatina sine Eruptione, Lancet, London, 1870, i, 227.
11. Dreyfus, Brisac: De la scarlatine anormale, à propos de trois cas observés dans la même famille, Gaz. hebd. de mèd., 1884, Series 2, xxi, 606.
12. Wetherill, Horace G.: A Series of Unusual Cases of Scarlet Fever, Tr. Med. Soc., New Jersey, 1888, p. 225.

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Furthermore Gosebler[13] in 1881 made a diagnosis of scarlatina in two children aged 30 months and 6 years respectively, despite the fact that they had no eruption, desquamation or throat symptoms. He based his diagnosis on the following grounds: that the children were ill for some time. the illness in each case being with fever and repeated vomiting, followed later by large amounts of albumin in the urine; and that it was at a time when scarlet fever was very prevalent in the town and quite fatal. Furthermore several cases of scarlatina without exanthemata had been observed. In 1892 Baiss[14] reported three cases in one family with the following history: The first child was found to have a temperature of 102; the next day the temperature was normal, but the child had a slight sore throat and some enlargement of the glands of the neck; otherwise it seemed to be well. There was desquamation later, however, and a few days after the beginning of the child's illness a second child was seized with more severe symptoms, and with an eruption which resembled measles. At this time the third child became ill with a typical scarlatinal eruption accompanied by jaundice. Were it not for the last case it would have been difficult to diagnose correctly those preceding.

Lee[15] reports sixteen cases, occurring in four families in which four adults and twelve children inhabited the same building. The series is noteworthy because of the absence of the exanthem as well as some other symptoms. In the first two only was any rash observed. The first patient when seen had a fast pulse, temperature 101, strawberry tongue, characteristic rash and sore throat. In five patients the glands were neither swollen nor tender. Only three had sore throat and only two vomited. The temperature in all ranged from 101 to

13. Gosebler, A.: Kurzer Bericht über drei Fälle von anomalen Verlaufe der Scarlatina, Prag. med. Wchnschr., 1881, vi, 385.

14. Baiss, J. R.: Some Anomalous Cases of Scarlet Fever, Boston Med. and Surg. Jour., 1892, cxxii, 630.

15. Lee, W. R.: Med. News, Philadelphia, 1892, p. 186, Scarlatina sine Exanthemata.

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102; the pulse in the children, from 140 to 148, and in adults from 130 to 134. The following sequelæ were noticed: One patient developed diarrhea, two bronchitis, and in two only was there desquamation. In two after some exposure there followed swelling of the submaxillary glands with rise of temperature and accelerated pulse. One woman, contracting the so-called scarlatina five days after labor, had puerperal fever.

Warry[16] reported an interesting epidemic of 150 cases of scarlatina with sore throat but with an absence of rash. The entire epidemic both in regard to those having rash and those without rash were found to be due to the milk supply. The author believed the cases without an exanthem to be scarlatina for the following reasons:

1. Many of the patients had desquamation during convalescence.
2. Others had kidney complications.
3. Several had arthritis.
4. Several developed otitis.

Further, it may be interesting to note that scarlatina without fever has also been recognized not infrequently and corresponds more or less with some of our cases.

D'Amore[17] reports several cases and Brunard in the past year states that he has observed a number of cases about Brussels. He mentions in particular three cases, in children, which occurred in one family. They ran an afebrile course and were mild, yet all three had typical scarlatina complications.

McClanahan[18] at Woodhull, Ill., also had the opportunity of studying afebrile scarlatina in a series of 150 cases. Many of his cases also were notable on account of the absence or mildness of the exanthem and other symptoms.

16. Warry, J. K.: Special Report on a Recent Outbreak of Scarlatina and Sore Throat Disease in Upper Clapton, Practitioner, London, 1892, xlix, 63.
17. D'Amore, L.: Scarlatina apiretica, contribuzione alla casuistica, Progresso med., Naples, 1895, ix, 25.
18. McClanahan, W. S.: Some Peculiarities in a Mild Epidemic of Scarlet Fever, Peoria Med. Jour., 1896, i, 339.

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He says that in December, 1892, he was called to see a patient with a temperature of 101, pulse 100, restless and complaining of itching. She had red faucial and buccal membranes; the tonsils had a fibrinous deposit over them, no strawberry tongue. By the next day restlessness had disappeared but there was a typical scarlet fever eruption although the temperature and pulse were normal. In another twenty-four hours the throat was clear, the rash and all other evidences of scarlatina had disappeared and the patient had no further trouble.

From this time until 1893 he saw about 150 cases. The fauces were involved in every case, as was the presence of the strawberry tongue. In about one-third of the cases there was no eruption. In six of them it resembled that of rubeola and in three the surface was nearly scarlet, red, smooth and glossy but without the minute points seen in the scarlatina rash. In the remainder the exanthem was the ordinary scarlet fever rash except that its stages were of shorter duration.

Twenty of the cases were followed by otitis; this occurred irrespectively of the other symptoms. The temperature seldom rose above 102, and this fever rarely lasted longer than three days; in fact, in the majority, the temperature was normal by the third day. At times the disease appeared to be contagious, at other times not.

Rodger y Piza[19] had the opportunity of observing an interesting case. In a certain family there was a child who ran through a typical course of scarlatina. Rodger y Piza was suddenly called in to see a younger child who had had a high fever for twenty-four hours and was voiding dark urine. The latter on examination was found to contain blood, epithelial cells, casts and much albumin. The hematuria lasted for thirty days. On the twelfth to the fourteenth days there occurred a

19. Rodger y Piza, Ramon: Un caso de escarlatina frustada, Rev. balear. de cien. med., Palma de Mallorca, 1903, xxiv, 27.

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slight furfuraceous desquamation on the face and upper part of the chest and forearms. From the presence of scarlet fever in the house Rodger y Piza had not the slightest doubt that this was a case of scarlatina *fruste*, so called by Trousseau, only one symptom of scarlet fever being present.

THE VARIATIONS OF SCARLET FEVER

From the foregoing it seems evident that what is known as scarlet fever varies greatly in its clinical manifestations. In a violent form it may cause death within a few hours, or in its mildest form it may be evanescent and difficult to recognize. As to the *materies morbi* which gives rise to scarlet fever we know nothing positively, nor of its mode of invasion. From the epidemics herein reported as well as others cited it would appear that the toxin varies in different outbreaks. From our observation it does not appear that mild infections beget malignant strains, or the reverse. Furthermore it should be remembered that in epidemics of a severe type atypical cases occur as frequently as in those of mild type.

From the fact that the tonsils are involved at a very early stage, and from the constancy with which this symptom has been noted, it would seem that the infecting agent gains access through these glands, as claimed by Dawson[20] and Lemoine.[21]

It seems unwise, therefore, with our imperfect knowledge concerning the etiology of scarlet fever, to regard these aberrant forms, which point strongly to some aberration of the exciting cause, as distinct affections. In 1894 Duke[22] endeavored to establish a "fourth disease" in the infectious exanthemata, but the consensus of opinion does not substantiate this claim. Our observations show that the most constant symptoms are

20. Dawson, W.: Med. Chron., Manchester, 1893-4, xix, 217.
21. Lemoine, G. H.: Bull. et mém. Soc. méd. d. Hôp. de Paris, 1895 and 1896; Gaz. Hôp. de Paris, Nov. 25, 1895, p. 1337.
22. Duke, Clement: Lancet, London, 1894, i, 791.

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the angina and slight nephritis, while an increase of eosinophiles in the blood was observed in a considerable number of our cases. Other phenomena are usually present even in atypical forms of the disease, but they are inconstant and subject to wide variation.

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ABSTRACT OF DISCUSSION

DR. W. L. BAUM, Chicago: I think that all of us who have had much experience with scarlet fever realize the great difficulty attendant on a correct diagnosis in these atypical cases. In Cook County Hospital in Chicago a number of cases have caused much controversy among the health authorities, the attending physicians and physicians in general practice. In attempting to reach a diagnosis in these cases, we have paid particular attention to the blood examination rather than to the local manifestations of the disease, and in our blood tests we have not laid so much stress on the absence of eosinophilia as on the differential blood count. We have elaborated somewhat on the theory propounded by Tillotson; that is, we have paid especial attention to the increase in the polynuclear nutritives. and so positive have we become that on that point alone do we exclude or admit the cases. We have had cases so mild that they would otherwise have escaped recognition. On the other hand, we have had cases in which the skin and throat manifestations were so manifest and pronounced that one would be led to the positive diagnosis of scarlet fever, and yet, on account of the presence of some other factor, such as a wound infection, a contrary diagnosis was established on the basis of the blood count. About three years ago I remember seeing a child with a small scalp wound, and at the same time there suddenly developed a slight temperature and sore throat, together with an erythematous rash commencing over the shoulder and extending to the sternum and other parts of the body. There seemed to be no question that the case was one of scarlet fever. When I saw the child on the following day, I was induced to make a blood count on account of the presence of the wound on the head, and as a result of the findings, scarlet fever was excluded. In the meantime, the child had been quarantined in the scarlet fever ward, and six days later it developed true scarlet fever, which proved fatal. I am convinced that it is on the basis of these blood counts that the differential diagnosis in these doubtful cases of scarlet fever can be made more positively than by any other means known at the present time.

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LICHEN NITIDUS

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In 1901 Pinkus described for the first time a peculiar papular eruption of the skin to which he gave the name "lichen nitidus." The affection was characterized by the presence of numerous flat-topped, shiny, pin-head-sized papules, which exhibited no tendency to grouping and never became confluent. The lesions were somewhat pinkish in color, and of practically the same hue as the surrounding skin. Their presence gave rise to no subjective symptoms, and often was discovered only by accident. The favorite seat of the eruption was the genital region, although the abdomen, breast and arms sometimes were attacked. In a later and more exhaustive article, contributed to the "Neisser Festschrift," Pinkus described in detail the clinical and histopathologic findings in nine cases of the affection.

Clinically, the eruption more nearly resembled that of lichen planus than of any other cutaneous disorder. The entire absence of itching, however, together with the distribution and color of the papules, and the fact that they never increased in size nor coalesced, distinguished lichen nitidus macroscopically. The shape, number, size and topography of the lesions served to differentiate them from verruca vulgaris.

In lichen scrofulosorum the disease has its seat about the pilosebaceous follicles, the papules are darker than those of lichen nitidus, and scaling is a prominent feature. Lichen scrofulosorum is an affection of childhood and adolescence, while lichen nitidus is usually seen in adults.

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Microscopically, Pinkus found the lesions to consist of hemispherical, granulomatous formations in the upper cutis, closely adherent to the epidermis, which was characteristically altered and greatly cornified. The granuloma resembled a tubercle. It consisted of a peripheral layer of round cells, with a center of epithelial cells, including a considerable number of giant cells of the Langhans type. The epithelial changes showed, especially in those lesions taken from the genital region, a central thickening of the rete, in the axis of which was a horny papilla, partly parakeratotic. This papilla was not constantly present, however. In the center of the granuloma, a minute abscess was sometimes found.

The layer of cylindrical cells and the pigment were lacking on the under surface of the epidermis. The upper layers of the granuloma were displaced by a horny coagulum and red blood corpuscles. No bacteria were found. No tests were made with tuberculin. Although the disease did not respond very favorably to treatment. in some instances (the patients being syphilitic) the eruption faded and even completely disappeared following the administration of mercury.

Recently, Arndt, working in Lesser's clinic in Berlin, has reported the findings and conclusions resulting from a careful study of twelve examples of the disease. In addition to these, he describes a thirteenth, in a middle-aged male, which he saw and diagnosed at the Hospital St. Louis, in 1904, and likewise discusses Lewandowsky's and Jadassohn's cases.

Lewandowsky's patient was a syphilitic man, aged 51, in the tertiary stage. The lichen nitidus lesions were on the back, arms and penis. Jadassohn's patient was also a man, 28 years old. The chest, back, legs and penis were involved.

In both of these cases the microscopic findings coincided with those described by Pinkus, except that the infiltration was localized around the ducts of the sweat glands.

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Arndt's patients all were males, from 12 to 45 years old (the average being 29), and of the twelve, six had had syphilis. In every instance the shaft of the penis was the seat of a greater or less number of the characteristic, sharply defined, pin-head-sized, flat-topped, shiny, flesh-colored papules. In four of the cases other regions also were affected. One patient, a waiter, aged 45, had lesions on the buccal mucous membrane. All the patients were ambulatory, and no tuberculin tests were made.

Pathologically, Arndt found that the changes were practically confined to the epidermis and the upper part of the corium. Surrounding the lesion, the rete cells were distinctly outlined, although somewhat separated from each other by the edema. The prickle cell and horny layers showed nothing abnormal.

In the diseased area the basal cell layer was absent. The lesion was oval in shape, and the infiltration was more dense in the lower than in the upper portion of the growth. The under surface of the epidermis, which formed the covering, was either smoothly bowed or roughly irregular in outline. In the center was often an epithelial projection which dipped into the infiltrated area below, and was invaded by many leucocytes. No connection could be shown to exist between this knob and the sweat-gland ducts.

Around this lesion the lymph channels were much widened, and bordered by a reticular stratum. This peripheral portion was quite rich in capillaries (in some instances with widely dilated channels), which penetrated the growth, but were lost toward the center. Here and there in the endothelium of these capillaries were seen karyokinetic figures. Connective tissue was present only in fine reticulæ, and an occasional bridge of collaginous tissue was found. No tubercle bacilli could be discovered. Peripherally, there were many darkly staining cells, among them giant cells with dark nuclei and homogenous or granular protoplasm. In the center were

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a few small, intensely stained, more or less irregular round cells, with little or no protoplasm. Arndt concluded that the histologic structure of the lesion was that of an infectious granuloma. In view of the fact that all special search had been without result, however, he stated that the identity of the causative agent was still in doubt. He considered the affection non-syphilitic in origin. Although special stains for the tubercle bacillus had failed to show the presence of that organism, Arndt believed that inoculation experiments might prove positive. He regarded the condition as probably tuberculous in nature—an atypical form of tuberculosis of the skin or a tuberculide.

Kyrle's case has recently been reported by Kyrle and McDonagh; the patient was a girl, aged 18. The regions affected were the flexor surfaces of the joints, especially the wrists and elbows, the axillæ and the anterior axillary folds, the inguinal regions and the genitocrural folds, the popliteal fossæ and the malleolar surfaces. There were also a few lesions on the neck, thorax and abdomen, and on the skin of the labia majora. The papules were typical in shape, size and color, and gave rise to no subjective symptoms. There was no glandular involvement, and a careful examination of the internal organs showed nothing abnormal.

The patient had had the disease since she could remember, and no alterations or periodical changes had ever occurred. An injection of 1 mg. of Koch's old tuberculin gave a rise of temperature from normal to 100.9 F., but without local reaction on the eruption.

Histologically, the skin, except where the nodule was situated, was normal. There were present no inflammatory changes in the cutis or subcutis.

The lesion itself consisted of a sharply circumscribed, ball-shaped mass of epithelioid and round cells, pressed closely against the epidermis. There was no definite arrangement of these elements, and no encircling loop of small round cells. Langhans giant cells also were present. No signs of caseation were to be seen.

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The vascular changes were similar to those met with in a typical granuloma. No capsule could be found. The overlying epidermis was characteristically altered, many of the cells having become separated from their mother position and appearing in the infiltration. No elastic fibers could be found directly under the epidermis. No tubercle bacilli were to be seen. Animal experiments proved negative.

Kyrle and McDonagh consider their case histologically identical with those of Pinkus, whose description of an individual lesion they quote as follows: "A small tubercle with its surface pressed against the epidermis and a tubercle in which no caseation occurs." They conclude that "the disease is a cutaneous lesion, probably brought about by a tubercular toxin, and characterized by the formation of a granuloma devoid of the usual inflammatory changes."

In addition to the twenty-five cases of lichen nitidus that have been reported, I desire to place on record the clinical history and laboratory findings in an example of the disease which has been under my observation during the past four months.

REPORT OF CASE

History.—The patient, E. G. G., male, is a railway passenger agent, aged 35, unmarried. Father died at 61, cause unknown; mother living and well at 73; one brother died of tuberculosis; two brothers and two sisters are living, all in good health. The patient's general health has always, with one or two exceptions, been excellent. He has had two attacks of gonorrhea. In 1906 he was operated on by a Chicago surgeon for a suppurating tuberculous gland in the left cervical region. The wound healed in less than a month, and subsequently has given no trouble.

Present Illness.—The skin eruption was first noticed in November, 1909. It gave rise to no subjective symptoms, and its presence was discovered by accident. The patient does not know how long it had existed.

Examination.—The patient is a large, broad-shouldered individual, 5 feet 11 inches tall, and weighs 205 pounds. A careful general examination fails to reveal any abnormal condition of the internal organs. The chest expansion is three and one-half

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inches, and the lung sounds are clear. On the left side of the neck is the scar left by the operation, and there is still perceptible enlargement of the underlying glands. The subcutaneous structures elsewhere are apparently not involved, however. There is a decided reaction to tuberculin (von Pirquet). The Wasserman (Noguchi) test gives a negative result. The buccal mucous membrane is normal.

On either side of the chest, just below the anterior axillary fold, is an oval of flat-topped, shiny, pin-head-sized papules. They are of the same color as the surrounding skin, and by the casual observer might pass unnoticed. In fact, the patient himself was unaware of their existence until his attention was called to them during the course of the examination. The tops of the lesions are smooth and burnished, and polygonal in outline. All are of practically the same size. There is no scaling nor crusting. Their arrangement is irregular, and there is no tendency toward coalescence. The patch on the right side consists of twenty or more papules, and the one on the left about thirty. Similar, but larger, affected areas are found in the groins. Surrounding the umbilicus is a ring-shaped collection, made up of eighty or more lesions. The lower extremities are free. There is a small collection of papules on the upper, anterior surface of each forearm, forming an oval patch on the left, and an enlongated tract on the right limb. The flexor surfaces of the wrists are the sites of numerous papules (these were the ones first noticed by the patient). The arrangement is similar on the two sides, and there are between 300 and 350 on each of the affected areas. The extensor surfaces of the thumbs also are involved. Generally speaking, the distribution of the lesions is roughly symmetrical, and very suggestive of lichen planus.

Histology.—For microscopic purposes, one of the papules on the anterior surface of the left wrist was excised and, later, three other lesions were removed from the right wrist. The tissue was fixed and hardened in alcohol, imbedded in paraffin, and serial sections made. For staining purposes, hematoxylin-eosin, polychrome methylene blue (Unna-Pappenheim), and carbol-fuchsin preparations were used, with Weigert's for elastic tissue. Under the low power, the lesion appears as an oval, egg-shaped granuloma, lying between the corium and the epidermis, and having its long axis parallel with the line which separates these structures. In none of the growths was the affected area associated with, or in close proximity to, a pilosebaceous follicle or a sweat-duct. Both of the major layers of the skin are altered in the immediate vicinity of the granuloma. That portion of the epidermis which forms the roof of the

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lesion is composed of a somewhat thickened stratum corneum, and several layers of tightly compressed and flattened nucleated cells from the stratum granulosum, the tumor being pressed closely against the under surface of this shell. There is no central epithelial projection, such as was found by Pinkus and by Arndt in some of their cases. The interpapillary plugs which form the outer boundary of the lesion are longer than those in the neighboring unaffected regions, and are pressed outward in such a manner that the under surface of the epidermis covering the granuloma forms a long, smooth bow which extends from the tip of one plug, over the end, top, and opposite end of the growth, to the tip of the interpapillary process which bounds the other extremity. Within the lesion there are irregular masses of degenerated epithelioid cells (with poorly stained nuclei), and a considerable number of small round cells with large, deeply staining nuclei. Of the papules examined one contained two Langhans giant cells, and one three. All were near the centers of the lesions. No evidences of caseation are to be found. An occasional slender reticulum of connective tissue is seen. The specimens stained for elastic tissue show no fibers in the central part of the lesion, but at one end, running along the periphery almost to the upper pole, several strands of this tissue are plainly visible. This arrangement of elastic fibers, which has not been noted by previous observors, is present in sections from both of the papules examined, although much more plentiful in one than in the other. The presence of these fibers may be readily explained if one considers that the growth originated at the side of the tip of a papilla, and progressed in such a manner that some of the marginal elastic fibers were cut off by the advancing granuloma, and being more resistant than the neighboring epidermal cells, were pushed upward and outward against the limiting wall. The fact that the papillary plug at this end of the growth is much shorter than the one opposite—because of less irritation and consequent stimulation, with succeeding cell proliferation—strongly favors this hypothesis. The capillaries are widely dilated just before they leave the corium, a peculiarity which is partly explained when their course upward is traced for a distance equivalent to about one-third the diameter of the lesion. Immediately after crossing the rather indistinct dividing line, and entering the granuloma, the walls become thicker—apparently a result of endovascular changes—and soon are blocked practically altogether.

Two of the excised papules were used for inoculation purposes. The bits of tissue, which had been removed under strict aseptic precautions, were placed in sterile salt solution and

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ground up in a mortar. The resulting mixture was injected into the inguinal regions of two healthy guinea-pigs. Up to the present time (four months having elapsed) the results are negative.

Treatment.—The results secured by treatment in this case are of interest. At first, the patient was given a mixture of menthol, thymol, chloral hydrate, oil of eucalyptus, chloroform and alcohol, to be used locally, and a tonic (biochemic) to be taken internally. Five weeks later, the eruption meanwhile remaining practically unchanged, an ointment containing salicylic acid and resorcin in vaselin, was ordered, its use to be alternated with benzoinated zinc oxid ointment. Within four weeks the skin was practically free from lesions. The patches on the right wrist and the right arm were the last to show improvement, probably because of the inconvenience experienced by the patient in applying the remedy with the left hand. At present there is scarcely a trace of the disease remaining.

It would be interesting to examine some of the areas that formerly were affected and note the changes that have taken place. It was with this object in view that several of the papules were carefully circumscribed with indelible ink before treatment was instituted. The patient objects, however, to further biopsies.

CONCLUSIONS

My conclusions may be briefly summarized as follows:

Lichen nitidus is a chronic, papular disease of the skin, probably tuberculous in origin, and characterized by the presence of minute, painless, flat-topped, shiny, flesh-colored lesions which exhibit no tendency toward grouping, and never become confluent.

Histologically, the lesion is a granuloma (not a tubercle), which originates in the tip of a papilla, and, as it gradually increases in size, follows the lines of least resistance and grows upward into the epidermis, shutting off and enclosing any projecting cell masses that may result from pressure or from cell overgrowth.

I am deeply indebted to my associate, Dr. J. Phillip Kanoky, for the privilege of making this report. Dr. Kanoky considers the case an example of lichen scrofulo-

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sorum. My diagnosis of lichen nitidus has been concurred in by Dr. William Allen Pusey of Chicago, who has seen the patient and examined the microscopic preparations, and by Dr. Charles J. White of Boston, who was kind enough to write me regarding the sections, some of which were presented to him.

I am also under obligations to other friends for courtesies rendered, to Dr. O. L. Castle, pathologist at the General Hospital, to Prof. A. H. Barber of the University of Kansas, and especially to Dr. W. K. Trimble, professor of pathology in the University of Kansas, for his kindness in doing the Wassermann (Noguchi) tests.

ABSTRACT OF DISCUSSION

Dr. J. A. Fordyce, New York: I have recently observed a case which may throw some light on the etiology of this condition. Histologically, it gave much the same picture. There were collections of giant, lymphoid and epithelioid cells. In the beginning the case showed small, pale papules, which clinically looked not unlike lichen planus. Later true tuberculous lesions developed and the patient died of a general tuberculosis.

Dr. R. L. Sutton, Kansas City, Mo.: One of our foremost dermatologists diagnosed this as a case of lichen planus, and not until he had examined the sections did he recognize the true condition.

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LICHEN PLANUS SCLEROSUS ET ATROPHICUS (HALLOPEAU)

A REPORT OF SIX CASES (FIVE NEW) WITH A REVIEW OF THE LITERATURE

OLIVER S. ORMSBY, M.D.
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The literature of this subject betrays some confusion as to what is meant by the term "lichen planus sclerosus et atrophicus."

Hallopeau first described this condition, named it "lichen planus atrophicus," and later added the word "sclerosus" to the title. Crocker added the word "morpheacus" on account of the resemblance in certain instances to morphea. That the disease resembles morphea to a marked degree is evidenced in the cases of Stowers, Allen, Schamburg, and others. These patients, when exhibited before dermatologic societies, were considered by some to be instances of lichen planus sclerosus et atrophicus, while others classed them as morphea.

There are some cases recorded under this title that appear to be of the ordinary lichen planus type, exhibiting subsequent atrophy of papules, leaving white atrophic spots. These are not examples of the type to be described here.

In 1887 Hallopeau[1] described the first case, and subsequently added three, one in 1889,[2] another in 1896,[3]

1. Hallopeau: Lichen Planus Atrophicus, Union méd., 1887; abstract by Thibierge, Ann. de dermat. et de syph., 1887, Series 2, viii, 790.
2. Hallopeau: Lichen Planus Sclerosus, Ann. de dermat. et de syph., 1889, Series 2, x, 447.
3. Hallopeau: Lichen Planus Atrophicus: a New Case, Ann. de dermat. et de syph., 1896, Series 3, vii, 57.

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and a fourth in 1898.[4] The histopathology of Hallopeau's first case was studied and reported by Darier; and subsequent observers have confirmed the original clinical and histologic descriptions of these two authors.

In 1892 Darier[5] fully described a similar case of his own.

In 1900 Crocker[6] transcribed notes taken by himself of a case presented by Morrant Baker before the London Dermatological Society, in 1882. In a chronologic order other recorded cases are the following: 1894, Brault[7] and Pawlow;[8] 1895, Gaucher, Barbe and Balli,[9] and Schwimmer[10]; 1896, Stowers,[11] Vinrace[12]; 1898, Vollmer[13]; 1899, Orbeck[14]; 1900, Zarubin[15]; 1903, Reiss,[16] and Wechselmann[17]; 1905, Allen[18]; 1906, von Zumbusch[19]; 1907, Montgomery and Ormsby,[20] Schamberg[21];

4. Hallopeau: Lichen Planus Sclerosus; a New Case, Ann. de dermat. et de syph., 1898, Series 3, ix, 358.

5. Darier: Lichen Planus Sclerosus, Ann. de dermat. et de syph., 1892, Series 3, iii, 833.

6. Crocker: Lichen Planus; Its Variations, Relations and Imitations, British Jour. Dermat., 1900, xii, 421.

7. Brault, F.: Un cas de lichen plan symmétrique à forme scléreuse amplifiée, Ann. de dermat. et de syph., 1894, Series 3, v, 834.

8. Pawlow, T.: Ein Seltener Fall von Lichen scleroticus ruber atrophicus, abstr. in Arch. f. Dermat. u. Syph., 1895, xxxii, 423.

9. Gaucher, Barbe et Balli; Lichen plan atrophique pigmenté, Ann. de dermat. et de syph., 1895, Series 3, vi, 302.

10. Schwimmer, E.: Lichen ruber planus atrophicans, Arch. f. Dermat. u. Syph., 1895, xxxiii, 451.

11. Stowers: Tr. Third Internat. Cong. of Dermat., 1896, p. 906.

12. Vinrace: Tr. Third Internat. Cong. of Dermat., 1896, p. 906.

13. Vollmer, E.: Ein Fall von Lichen planus ruber mit linearer Hautatrophie, Dermat. Ztschr., 1898, v, 32.

14. Orbeck, W.: Lichen atrophicus und Vitiligo, Arch. f. Dermat. u. Syph., 1899, i, 393.

15. Zarubin: Lichen atrophicus, Arch. f. Dermat. u. Syph., 1900, li, 306.

16. Reiss, W.: Uber atrophische Formen des Lichen planus, Arch. f. Dermat. u. Syph., 1903, lxviii, 137.

17. Weschselmann: Lichen ruber atrophicans, Arch. f. Dermat. u. Syph., 1903, lxviii, 446; Ueber Lichen atrophicus und andere makulose atrophien der Haut, Arch. f. Dermat. u. Syph., 1904, cxxi, 333; Atrophoderma Erythematosa maculosa (Lichen planus atrophicus), Dermat. Ztschr., 1904, xi, 28.

18. Allen: A Case of Lichen Planus Atrophicus, Jour. Cutan. Dis., 1905, xxiii, 266.

19. Zumbusch, von: Lichen Albus, Arch. f. Dermat. u. Syph., 1906, lxxxii, 339.

20. Montgomery and Ormsby: White-Spot Disease (Morphea Guttata) and Lichen Planus Sclerosus et Atrophicus, Jour. Cutan. Dis., 1907, xxv, 1.

21. Schamberg: Lichen Atrophicus, Jour. Cutan. Dis., 1907, p. 578.

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1909, Hoffman,[22] Riecke,[23] Millian,[24] and Csillag.[25] The majority of the above cases are typical; the exceptions will be discussed later.

SYMPTOM-COMPLEX

The symptom-complex constituting the disorder as originally outlined by Hallopeau and confirmed by numerous observations since, includes the following:

The major portion of patients have been women varying in age from 30 to 63 years. They have usually been of nervous temperament. No other important fact has been demonstrated relative to the etiology. The sites of predilection are the upper portions of the trunk, about the breasts, over the clavicles, extending over the shoulders and downward over the upper part of the back, also the neck, axillæ, and forearms. Lesions also have been noted over the abdomen, on the thighs, about the vulva; and coincident lesions were noted by Hallopeau on the buccal mucosa, and in one case in this report, on the vaginal mucosa. The temple was affected in one of the atypical cases. (Dubreuilh and Petges).[26]

The characteristic lesion is an irregular, often polygonal, flat-topped, white papule. In the case of Morrant Baker, some conical papules were noted. The white color of lesions is striking and has been compared with that of ivory and mother-of-pearl. At times a distinct yellowish tinge is noted. The papules, as a rule, are firm to the touch, neither elevated nor depressed, but

22. Hoffman, E.: Ueber einen mehrere Jahre hindurch beobachtetan Fall von Lichen Sclerosus, Ikon. Dermat., 1909, Fasc. iv, Tab. xxvii-xxxv.

23. Riecke, E.: Zur Kenntnis der Weissfleckenkrankheit, Arch. f. Dermat. u. Syph., 1909, xcix, 181.

24. Millian, M. Y.: Lichen plan atrophique on mieux leucodermie atrophique ponctuée, Bull. de la Soc. française de dermat. et de syph., 1909, No. 7, p. 279.

25. Casiliag, J.: Dermatitis Lichenoides Chronica Atrophicans (Lichen Albus von Zumbusch), Ikon. Dermat., 1909, No. 4, Tab. xxxii-xxxv, p. 147.

26. Dubreuih and Petges: Lichen planus atrophicus, Ann. de dermat. et de syph., 1907. Series 4, viii, 715. (A complete clinical report of a case with abstracts of seven other cases and a discussion of additional ones.)

27. Stein, R.: Ueber Nævus anæmicus, Arch. f. Dermat. u. Syph., 1910, ci, 311. The author refers to the previously recorded cases of Vorner in 1906 and Fischer in 1909.

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slight elevation may be present. They bend with the skin and when grouped may become wrinkled. As a rule, no areola is present, but at times a rosy or moderately pigmented zone surrounds the papule. They may be discrete or grouped and most cases present both types. When grouped to form plaques, the outline of the individual papules forming the plaques can be determined.

Each papule has on its shining, smooth surface from one to several (sometimes as many as twenty (Darier)) black or dark horny, comedo-like plugs, or minute pit-like depressions, which show the former site of the horny plugs. These elements are situated at the pilo-sebaceous or sweat-pore orifices, and are most important from the viewpoint of diagnosis. The wall of the pit-like depressions is of the same nature as the horny plug. The plaques vary in size up to several centimeters in diameter. They show on their surface the outlines of the primary papules containing the horny plugs, or exhibit minute depressions; and the whole plaque shows the peculiar shining white surface characteristic of the primary lesions. A linear arrangement of the papules is at times noted, similar to that seen in ordinary lichen ruber planus. There is, as a rule, no clinical sign of inflammation. The mode of development, as described by one of Hallopeau's patients, is as follows:

> A black, horny point, surrounded by a bright red areola, is first noted. New and similar points occur which, after some months, unite; then the horny plug falls and the plaque becomes white.

My observations have not been similar, as I have seen new lesions developing, and the earliest manifestations consists of a minute white papule at the beginning, with either a dark spine or a pit on the surface.

The lesions, both papules and plaques, are persistent, but after a variable time, either from treatment or spontaneously, they undergo resolution and leave a delicate, smooth, white, soft, atrophic area of the size and shape of the original lesion, whether it be a discrete papule or

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a larger plaque. In one patient seen two years after complete involution of the lesions the atrophic scars were still present. The subjective sensations vary. Itching is the rule, but it is usually moderate in grade. A pulling or drawing sensation is described by some patients, while in others no subjective sensations are present.

HISTOPATHOLOGY

The changes described originally by Darier in Hallopeau's case have been confirmed by many observers. The most important change noted is a sclerosis of the papillary and subpapillary layer of the corium. In general the resemblance in the histologic architecture between this condition and ordinary lichen planus is marked. The stratum corneum is thickened, as is also the stratum granulosum in most instances, while the rete is atrophied. The wavy line between the rete and the corium is straightened or obliterated. The entire upper portion of the corium shows marked collagenous hypertrophy. The collagen bundles are condensed and show less of the interlacing characteristics than usual. Very few connective tissue nuclei are present. The elastin is reduced in amount. A cellular infiltration is present, deeply in the corium, and moderately also about the vessels, glands and folicles. Horny plugs are described in the sweat-pores, extending into the ducts, and the latter show a condition of hyperkeratosis. Similar horny plugs have been described in connection with the pilo-sebaceous orifices.

From ordinary lichen planus this condition is distinguished by the presence of marked sclerosis in the upper part of the corium, and by deeper situation of the inflammatory process.

DIAGNOSIS

The important point in differential diagnosis is to distinguish this disorder from morphea guttata or circumscribed scleroderma. Vitiligo and nevus anemicus[27]

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Fig. 1; Case 1.—Lichen planus sclerosus et atrophicus, showing discrete whitish papules and plaques with black horny points on the surface. Courtesy of *Jour. Cutan. Dis.*

Fig. 2; Case 1.—Lichen planus sclerosus et atrophicus. Showing one plaque shown in Figure 1. Courtesy of *Jour. Cutan. Dis.*

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Fig. 3.; Case 1.—Lichen planus sclerosus et atrophicus. Showing a higher magnification of one area shown in Figures 1 and 2.

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would cause no confusion. The so-called "white-spot disease" should be mentioned, but as the cases of this disorder are most, if not all, examples of circumscribed sclerodermia, no further comment is necessary. The irregular or angular, flat, shining, white papule, having on its surface dark, horny plugs or minute depressions, is characteristic of lichen planus sclerosus. Circumscribed scleroderma is not characterized by papules, and the horny plugs or punctate depressions are absent. These facts hold true for the most minute spots, as well as for large plaques. Lichen ruber planus with atrophy is distinguished by the presence of the ordinary red papules, and usually by severe itching, the latter, in the disorder under consideration, being slight or absent. There are no white papules, but merely atrophic white areas, which are secondary to a former inflammatory process.

SUMMARY OF RECORDED CASES

The majority of cases mentioned earlier in this article are pure examples of the Hallopeau type. A few only will be briefly discussed.

Von Zumbusch's case of "lichen albus" is classed here as belonging to the Hallopeau type.

Csillag's case of dermatitis lichenoides chronica atrophicans probably belongs here, as does also Millian's case of lichen planus atrophicus, for which he thought the best title would be "leukoderma with punctate atrophy."

Riecke's case of provisional "white-spot disease" practicaly fulfils the requirements of this group. On the other hand, the case of Dubreuilh and Petges (lichen planus atrophicus), that of Gaucher, Barbe and Balli (lichen planus atrophicus et pigmentosus), and that of Wechselmann, of atrophodermia erythematosa maculosa (lichen planus atrophicus), and Pringle's case (annular and atrophic lichen planus), are examples of lichen ruber planus associated with cutaneous atrophy.

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The case of von Zumbusch, described by him as a new disorder and termed "lichen albus," clearly belongs to this group. The clinical picture and histologic findings were later reviewed by Hallopeau,[28] who believed that it should be classed as a case of lichen planus sclerosus.

Under the title "dermatitis lichenoides chronica atrophicus" Csillag describes a case which he classes as analogous with von Zumbusch's lichen albus. The clinical description of the lesions in this patient correspond in many particulars to those found in the cases of the subject under discussion, and is, therefore, placed provisionally in this group. Pale red mixed with chalky-white small areas and large plaques are described, on the surface of which are horny plugs connected with the pilo-sebaceous openings. The plate used for illustration is less characteristic than the written description.

Millian describes a case under the title "lichen planus atrophicus," or, better, "leukoderma with punctate atrophy," in which pin-head to pea-sized white lesions occurred. These were circular, shining, depressed, and showed a central punctate opening, as though they had been pricked with a pin. The large plaques were white, waxy and scaling. The earliest lesions did not present the punctate depressions. There were no subjective symptoms aside from some drawing sensations, and no ordinary lichen planus papules.

In the discussion of this case Darier stated that the disorder could be classed in one of four categories: lichen planus sclerosus, white-spot disease, "scleroderma *en carte de visite*" of Unna, or lichen albus. It appears, therefore, reasonable to place it in the group under discussion.

The most interesting report of all recent ones is that of Riecke. He gives a careful clinical and histologic analysis of a case, critically surveys the literature on the subject and finally places his case provisionally with two

28. Hallopeau: The Nature of Lichen Albus of von Zumbusch, Bull. de la Soc. Française d. dermat., 1907-08, p. 106.

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others—those of Westburg[29] and Johnston and Sherwell[30]—under the title of "white-spot disease." On account of the very close resemblance to lichen planus sclerosus of his clinical and histologic description, as well as the plate used for illustration of the case, a brief abstract follows:

The patient was a woman, 50 years of age. The cutaneous disorder began ten years before with a lesion the size of a silver quarter over the pit of the stomach, preceded by itching. The lesions had extended rapidly during the previous year. On examination the following was noted: The lesions were located chiefly on the abdomen from the pit of the stomach to the inguinal folds with a few on the outer surface of the thighs. They were sago-grain to lentil-sized, well-defined, round, oval, irregular, and polygonal in shape, with many closely set and confluent plaques, largely on a level with the cutaneous surface. The smaller were slightly elevated, but, on the whole, they were neither elevated nor depressed. They were not palpable and presented a markedly white luster. Each had a central punctate depression resembling a comedo. The smaller were smooth and showed no sign of inflammation. In the center of an older area some color, red or reddish-brown, was noted. In some areas a thin brownish-red crust covered the lesion, but, as a rule, this was surrounded by an alabaster-white ring. In some of the areas was a white lesion surrounded by a red halo. By confluence nail-sized plaques were formed.

Histologically, the stratum corneum was thickened; the rete thinner than normal, and the wavy line between the epidermis and the corium was largely obliterated. The connective tissue of the corium was increased in amount and presented few nuclei in its bundles. A cellular infiltration was noted deeply and at the periphery of the area. Vacuoles and lacunæ were noted between the corium and epidermis, which the author deemed an important finding. The elastin that was present was normal. Horny masses were present in the hair follicles, extending as far as the sebaceous gland opening.

The case of lichen planus atrophicus described by Dubreuilh and Petges is not of the type under discussion. The lesions were situated chiefly on the forehead, in the scalp, and later in the mouth. During the course of the disease the question of diagnosis was uncertain

29. Westburg: Monatsh. f. prakt. Dermat., 1901, xxxiii, p. 355.
30. Johnston and Sherwell: Jour. Cutan. Dis., 1903, xxi, 302.

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for some time. Lupus erythematosus, syphilis and sclerodermia en plaque were considered. Finally, after the mouth lesions were discovered, the diagnosis above named was made. The case apparently was one of anomalous lichen planus associated with cutaneous atrophy.

The case of lichen planus atrophicus et pigmentosus of Gaucher, Barbe and Balli does not belong to this group. This patient exhibited highly-colored pruritic papules and plaques associated with marked hyperpigmentation, and, finaly, atrophy. When the case was discussed before the French Dermatologic Society, Darier, who was familiar with the Hallopeau type, was of the opinion that the case was not one of lichen planus sclerosus.

Wechselmann, in 1903, reported a case under the title "lichen planus atrophicus." This case was further described with detailed histologic study, in 1904, under the title "atrophodermia erythematosa maculosa (lichen planus atrophicus)." The patient was a man, 35 years of age, with cutaneous lesions situated on the forehead, in front of the left ear, over the mastoid region, in the hairy scalp, and on the back to the left of the spinous processes near the junction of the first thoracic vertebra. In the last-named region, bluish-red, umbilicated, ordinary lichen planus papules were described. In the regions about the temple, ear, and scalp, erythematous and papular lesions, forming patches, occurred, which later underwent atrophy. The histology is that of lichen planus with atrophy. No white papules were described, and the case clinically, as well as histologically, is not properly of the Hallopeau type, but appears rather to belong to the group in which atrophy was a sequence.

Pringle[31] exhibited a case of annular and atrophic lichen planus before the London Dermatologic Society in May, 1901. This was an example of ordinary lichen planus with atrophy.

31. Pringle: A Case of Annular and Atrophic Lichen Planus, Brit. Jour. Dermat., 1901, xiii, 215.

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Fig. 4.—Lichen ruber planus with associated subsequent atrophic whitish areas. Shown for comparison with lichen planus sclerosus

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Fig. 5.—Morphea guttata resembling lichen planus sclerosus et atrophicus. Back view of a patient who had diffuse scleroderma of the lower limbs. Reported in *Jour. Cutan. Dis.*, 1907.

Fig. 6.—Morphea guttata closely resembling lichen planus sclerosus et atrophicus (front view).

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Figure 4 illustrates a case of lichen ruber planus associated with circumscribed atrophic white areas. The case is cited merely for comparison.

The six cases recorded here occurred in the practice of Dr. James Nevins Hyde, the late Dr. Frank Hugh Montgomery and myself. Case 1 is reproduced from a report[32] made in 1907, for the reason that a microscopic study was made in that case. In the five new ones only clinical observations are available.

CASE REPORTS

CASE 1.—Patient consulted me at the West Side Hospital (dermatologic clinic), in January, 1906. "The patient, a woman, aged 56, was born and reared in Germany, but has lived in Chicago for thirteen years. She has had seven pregnancies, three of which terminated prematurely. In two others, the infants lived only a few hours, and the remaining two are represented now by two healthy children, aged 23 and 25 years respectively. She gives a history of having suffered many times during her life with a vague febrile disorder she called 'malaria.' She is very heavy, somewhat pallid, but fairly well nourished, and is excessively nervous.

"The present skin disorder began about eight months ago, she states, as small white and black spots, which have gradually increased in number. The lesions are now situated chiefly over the back part of the shoulders, but extend toward the neck and also a short distance down the back. A few spots are scattered over the upper part of the chest down to the margin of the mammæ, and there are a few lesions on the upper and external aspect of the arm.

"The primary lesion is apparently a slightly elevated, angular, polygonal or irregularly-shaped, white papule, which on attaining the size of a millet-seed shows on its surface one or several small, elevated, black, comedo-like points, or minute depressions, where the black points formerly existed. A lesion of the size of a split pea usually contains five or six such points or depressions. The papules vary in size from that of a pin-head to that of a split pea. A few very minute, angular, white papules are present. Some of the lesions are surrounded by a narrow, pinkish areola; others by a brownish discoloration; while many present no color changes at the border.

"Over the back part of each shoulder is a patch formed by the coalescence of papules which, however, do not completely

32. Jour. Cutan. Dis., xxv, 1.

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lose their identity. One of these patches measures about two inches in diameter, is irregular in outline, slightly elevated, white in color except for the black points and depressions which dot its surface, rough to the touch, and presents a somewhat wrinkled appearance (Figs. 1, 2 and 3). Over the upper part of the chest the lesions are discrete, irregularly disseminated and abundant. Over the clavicles a somewhat linear arrangement is apparent; while in other areas there is some grouping of the lesions. Here and there atrophic, slightly depressed lesions are present, which are of the shape and color of those just described.

"During the two months in which she has been under observation, there have been displayed at times a very few small, red- or brown-tinged papules, which were indistinguishable from the lesions of ordinary lichen planus, but their transformation into white papules could not be traced. During this period the patient has had very simple treatment, and the only change noted is the disappearance of most of the small, elevated, black points, their places now being occupied by the depressions. She complains of no subjective sensations except, as the patient describes it, that of 'pulling.' There are no lesions in the mouth or about the wrists.

"*Histology.*—A biopsy was performed, removing a split pea-sized lesion from the posterior aspect of the left shoulder. This lesion was typical and exhibited on its surface six small dots or depressions, from which the comedone-like plugs had been removed. The tissue was fixed and hardened in alcohol, embedded in paraffin, and stained in various ways. A series of sections in which two hair follicles occurred were studied. A lanugo hair was present in each follicle. The most marked changes are in and about these follicles. As a whole, collagen and elastin are abundantly present, except in the areas of cellular infiltration, where both are either lessened or absent. Aside from the special areas to be described, the collagen appears condensed and contains fewer connective tissue nuclei than normal. Blood-vessels are few and are represented by strings of cells running horizontally across the field or radiating in various ways from the hair follicles. No vessels can be demonstrated in the papillary layer. In these sections three distinct and fairly well defined masses of cellular infiltration are present, in addition to that surrounding the follicles. They are situated in the lower part of the corium, about parallel with the base of the follicles, but not in connection with these structures. Beside these deposits, some small areas and some single cells are irregularly distributed about the corium. The infiltration is composed of connective tissue cells, lymphocytes, or small plasma cells, and mast cells. The latter are unusually

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abundant and occur not only in these special areas, but also irregularly throughout the corium. They are of various shapes, some large with their granules extending far from the nucleus. The changes in the epidermis occur chiefly about the follicular openings. The line between the epidermis and the corium is fairly well defined, its wavy character being only in places obliterated. The rete Malpighii consists of about eight rows of cells, in which there is some increase in the pigment. The stratum granulosum is composed of two rows of elongated, flattened cells containing fine granules of keratohyaline material. The stratum lucidum is not demonstrable, and the stratum corneum is thickened. The mouths of the two follicles, above mentioned, are widely dilated, and in the section present the appearance of a deep v-shaped opening, extending from the surface into the follicle. In places in the different sections a part of this large opening is occupied by a horny material similar to the stratum corneum. The lanugo hair can be demonstrated in the center of this opening, extending down to the base of the follicle. No sweat-ducts or pores occur in the sections, making it impossible to determine a connection between these structures and the clinical pits or depressions. The coil glands present are unaffected. In one place is a circumscribed area of cellular infiltration in the corium between a coil gland below and the epidermis above, but it seems to have no relation to the gland or its duct. From the involvement of the pilo-sebaceous apparatus in such a pathologic process it would seem that this is the seat of the original comedone-like plug, and, later, the pit or depression. The pathological process is more deeply situated than in ordinary lichen planus and the marked involvement of the follicles is not usual in the common variety."

CASE 2.—A private patient of Dr. Hyde's, seen Oct. 15, 1906, and under observation for about two and a half years, was 49 years of age, weighed 176 pounds, and was not robust. The family history revealed no important facts. For years the patient had been nervous and slept poorly. She had suffered from variola at 5 years of age and had in addition the usual diseases incident to childhood. For twenty years she suffered from pruritus each summer, chiefly on the lower limbs. The cutaneous disorder began five years before, on the wrists and thighs. Six months before new lesions occurred about the vulva, accompanied by severe itching, and it was this that induced the patient to seek relief.

An examination on Oct. 15, 1906, showed, on the flexor surfaces of each wrist, many dense, white, irregular papules, varying in size, also some larger plaques. The former were poppy-seed to pea-sized; the latter somewhat larger than a coffee-bean. The inner faces of the thighs showed several round,

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oval or irregular areas, sharply defined, white or pale red, with a slightly depressed and atrophic center, the border being narrow and irregular, and consisting of small, dense, white, irregular papules. The surface of these lesions was shining and showed punctate depressions. A few scattered lesions were present over the abdomen, about the groins, and over the legs and arms. Some traumatic lesions were also present in these latter areas. On the mucous membrane of the vagina, especially about the clitoris, was a characteristic lichen planus infiltration.

Six months later the patient developed diabetes mellitus, which was still present when she was last seen. In April, 1909, there was a marked recurrence of the pruritus vulvæ, at which time typical lesions of lichen planus sclerosus in various stages of involution were present. A period of radiotherapeutic treatment was given in April and May, since which time the patient remained comfortable.

CASE 3.—The patient consulted my late colleague, Dr. Montgomery, May 31, 1907, from whose notes the following is taken:

The patient, Mrs. M. B., aged 33, had been a delicate, nervous child, but had had no serious illness except scarlet fever from which she had made a good recovery. After finishing a high-school course, she studied and later practiced law five years Ten years before, while studying, she noticed the first signs of the present skin disorder, which appeared as small white spots over the posterior surface of the shoulders. They were white in the beginning and had never been productive of any subjective sensations. They persisted with little or no change except to become somewhat more depressed. Six or eight months before this visit she noticed new areas coming on the back of the neck in the median line extending into the occiput. About one month later lesions began to appear over the breasts and on either thigh. After another month a small area appeared on the anterior surface of the neck (left side), and for about a month lesions appeared on the anterior surface of both wrists. On examination, an irregular triangular area on the back of the neck was typical of lichen planus sclerosus et atrophicus. Not only were the normal lines and folds of the skin exaggerated, but quite typical sclerotic lichen planus papules were visible. A number of these showed characteristic black points. The older lesions on the shoulders exhibited slightly depressed atrophic areas covered with parchment-like epidermis. They were white, but had a slightly dirty-yellowish tinge. On the anterior surface of the neck were a few papules, some with black points, and some showing atrophic areas. Two irregular areas about 2½ inches in

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Fig. 7.—Morphea guttata. Same patient as represented in Figure 6 (back view).

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diameter were situated on the outer surface of either hip, made up of minute atrophic points, some of which were distinctly angular in outline. On the anterior surface of each wrist were three or four pin-head-sized and smaller, whitish papules. Some of them had the appearance of being beneath the skin. These had been there about a month. Just above each nipple was an irregular area about 1½ inches in diameter made up of quite closely aggregated, clear, white, very slight depressed (?) atrophic points. In this plaque individual lesions retained their identity. No depression or change in texture could be detected with the finger. The patient and her husband (a physician) were positive that there had been no preceding changes of a different character, and that the patches enlarged simply by the appearance of new white points of the same character. Dermographism was marked and had been present for about a year. A report after seven months indicated no change in the existing, and no appearance of new, lesions.

CASE 4.—The patient, a woman aged 67, consulted Dr. Montgomery Oct. 16, 1907. No notes were made concerning the family history. Her general health was fair. She passed the climacteric period at the age of 45. She was of a markedly neurotic disposition. Her skin showed evidences of senility, being thin, atrophic, with patches of hyperpigmentation, and areas of keratosis. The cutaneous disorder was of five years' duration, and had been treated in Hanover, Germany. The patient had also consulted Professor Lassar, of Berlin.

The lesions were situated on the front and back of each shoulder and on the neck with a few outlying papules over the chest. The greater number of lesions were irregular white papules, level with the skin, on the surface of which were minute black points. There were also several typical atrophic areas where lesions had undergone resolution. Slight telangiectasia was noted in the region of some lesions, which varied in size from 2 to 4 mm. Early in the history of the disorder itching was quite marked; later it became less and at the time of the examination was present only to a slight degree. Six months after the first examination there was not much change in most of the lesions. The area on the right shoulder had increased in size. At this time a general examination revealed an interstitial nephritis, with albumin and casts in the urine and blood-pressure of 230. In addition to topical applications, radiotherapy was employed. In March, 1910, I again examined the patient, when only the relics of the lichen planus sclerosus lesions remained. The last consultation was made with reference to the facial hyperpigmentations.

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CASE 5.—The patient consulted me, Aug. 11, 1909. This patient was a refined, rather delicate woman, 42 years of age. Aside from her nervous temperament, no facts of importance relative to the family or past history were obtained. The cutaneous disorder was of fourteen months' duration. It began on the right side over the region of the clavicle, with six to eight pin-head-sized whitish papules. New lesions gradually developed over the shoulder and upper part of the back, and over the opposite clavicle, shoulder, and back, and a few sparsely distributed over the abdomen. On examination, individual, discrete, irregular, flat-topped, hard white papules, each presenting two to five dark, horny elevations on its surface, and in some only pit-like depressions, were noted in all the described areas. In addition, several dime-sized areas, especially over the shoulders, displayed characteristic grouping of the papules. In these areas individual papules could be detected. The surface was whitish, except where dotted with horny plugs or dark minute pit-like depressions. Radiotherapy was employed during September, 1909. In December, the lesions had largely undergone resolution. In April, 1910, two new plaques developed. In this patient no areola was ever present and no lesions suggesting lichen ruber planus. There was no vascular element in the case, and no mucous membrane involvement. The lesions were sclerotic and whitish from the minutest earliest to the older, forming plaques, each showing characteristic dark points.

CASE 6.—The patient first appeared at the dermatologic clinic of Rush Medical College, where she was seen by Dr. Anthony, through whose courtesy I saw her. This patient was the youngest of the group, being 30 years of age. She was seen first on Aug. 17, 1909. She was a telephone operator, highly nervous, had suffered for a long period with severe headaches, and frequent attacks of palpitation of the heart. She was not robust. Her hands and feet were habitually cold. The urine was normal, though she was annoyed by frequent urination. She was practically neurasthenic.

The cutaneous disorder was of one and a half years' duration, and was nearly a replica of Case 5 of this series. The lesions were situated over the clavicles on each side, and extended from over the shoulders to the upper part of the back. The same white sclerosed papules, discrete and grouped, all containing dark horny spines or minute horny depressions, were present. There were no red papules, none of the lesions had an areola, and there were no mucous membrane lesions.

This patient was demonstrated with Case 5 at a meeting of the Chicago Dermatological Society in December, 1909, at which

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several members of the American Dermatological Association were present.

In February, 1910, radiotherapy was used, with beneficial results.

SUMMARY OF THE SIX CASES HERE RECORDED

All the patients were women, aged 30, 33, 42, 51, 51 and 63 years, respectively. All were neurotic. One had neurasthenia; another had marked, peculiar psychic phenomena; diabetes was present in one; interstitial nephritis in a second. The duration of the cutaneous disease was eight months, fourteen months, eighteen months, five years, five years and ten years, respectively.

The site of most extensive involvement in five of the patients was the region over the clavicles, shoulders, neck and upper part of the back. In one the wrists, flexor surface, thighs, abdomen, groins, were chiefly affected, with a few lesions appearing on the legs and arms. The essential lesions in all cases were whitish, discrete, round, oval, irregular, or polygonal, flat-topped papules; similar lesions forming whitish plaques, all having dark, horny spines, or punctate depressions. The lesions were either level with the surrounding cutaneous surface or very slightly elevated. In all the terminal result was a white depressed, delicate scarring or production of atrophic areas of the size and shape of the preceding lesion, whether papule or plaque.

In two patients a few usual reddish lichen ruber planus papules were present, but they were never observed undergoing transformation into the white lesions. The latter were from the beginning white papules.

In one patient coincident mucous membrane involvement with ordinary lichen planus was noted. In Hallopeau's case this occurred in the mouth. In one of my cases the vagina was involved. In five cases subjective sensations were slight or absent; in one they were marked, but the pruritus could not be attributed to the disorder under discussion.

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That the disease may be persistent is evidenced by its long duration in some of the patients who still exhibit active lesions.

In five cases in which radiotherapy was used it proved to be a valuable therapeutic measure.

The group as a whole corresponds clinically with the Hallopeau type of lichen planus sclerosus, and in the one case where a histological study was made it corresponded with Darier's observations in Hallopeau's case, and also with his own.

CONCLUSIONS

From the brief summary detailed above it appears logical to group the six cases under one title. They do not differ from one another more than the members of any group of six different patients suffering with any single dermatosis. In the question of differential diagnosis only three cutaneous disorders capable of producing whitish lesions on the skin need be considered, viz.: localized or circumscribed scleroderma (Fig. 5), lichen ruber planus of usual type associated with or followed by atrophy, and the so-called "white-spot disease." Such disorders as vitiligo, syphilis, lupus erythematosus, naevus anaemicus, and lepra are readily excluded. Lichen planus of the usual type associated with atrophy is excluded by the fact that the primary lesion in these cases is never reddish, as in its whole career it is a whitish sclerotic papule. That these cases are probably of the same nature and simply a special form of lichen planus is strongly suggested by the association in certain cases with mucous membrane involvement of the lichen planus type; also by the fact that some papules of the ordinary form at times concur, and, finally, by the fact that the lesions themselves, both as to size, and arrangement, are similar, the striking difference existing only in the color and presence of characteristic dark, horny spines and keratotic punctiform depressions. The so-

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Fig. 1.—Senile keratosis (Zeiss 16 mm., C.O.4). Illustrating the thickened horny layer and corneous plugs of the pilo-sebaceous apparatus. In the rete and corium areas of degeneration.

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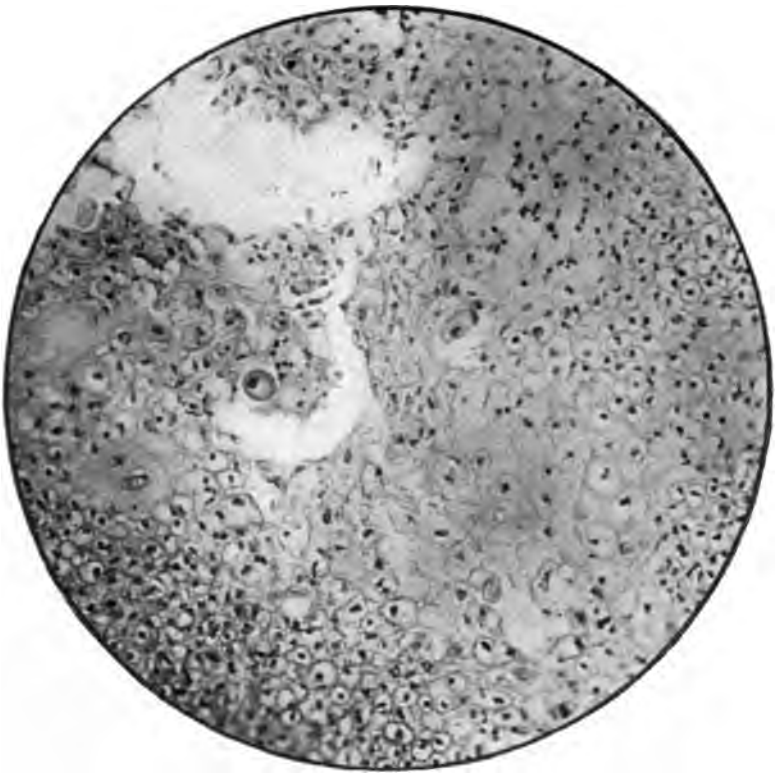

Fig. 2.—Senile keratoma (Zeiss 8 mm., C.O.4). Section of wart from back of hand of patient with epithelioma of finger and other senile changes in skin, as telangiectases and pigmentations. Main mass of wart made up of masses of large cells which have lost their prickles and show various degenerative changes in nuclei and cell body due to vacuolization and hyalin. Underneath growth zone of lymphocytes and plasma cells. Subepidermic connective tissue on either side degenerated and rarified.

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Fig. 3.—Xeroderma Pigmentosum (Zeiss 8 mm., C.O.4). Small warty growth, showing hypertrophied horny layer and rete. Many cells of latter show degenerative changes, are vesicular and have large deeply staining nuclei. Corium degenerated and dense infiltration occupies upper layers of cutis in close juxtaposition to epidermis.

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Fig. 4.—Xeroderma Pigmentosum (Zeiss 16 mm., C.O.4). Warty growth showing marked hypertrophy of all the layers, with hyalin degeneration and pearl formation in center of lesion. Corium shows degenerative changes and is seat of inflammatory exudate.

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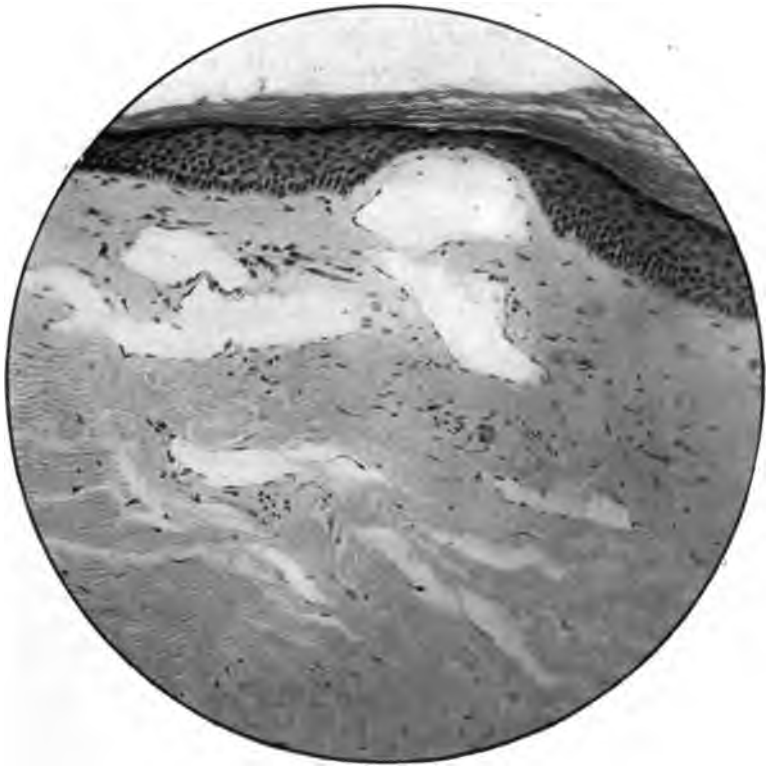

Fig. 5.—*X*-ray dermatitis (Zeiss 8 mm., C.O.4). Illustrating degenerative change in the corium, and tortuous capillary dilatation.

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Fig. 6.—Arsenical keratosis (Zeiss 8 mm., C.O.4). To show degenerative changes in cells and clumping of nuclei probably due to amitosis.

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Fig. 7.—Basal-celled epithelioma developing in a lupus scar (Spencer ½ in., Zeiss Proj. Oc. 2). Tumor consists of irregularly rounded, oval and elongate masses of small cells with central degeneration. There is no connection with the surface epithelium.

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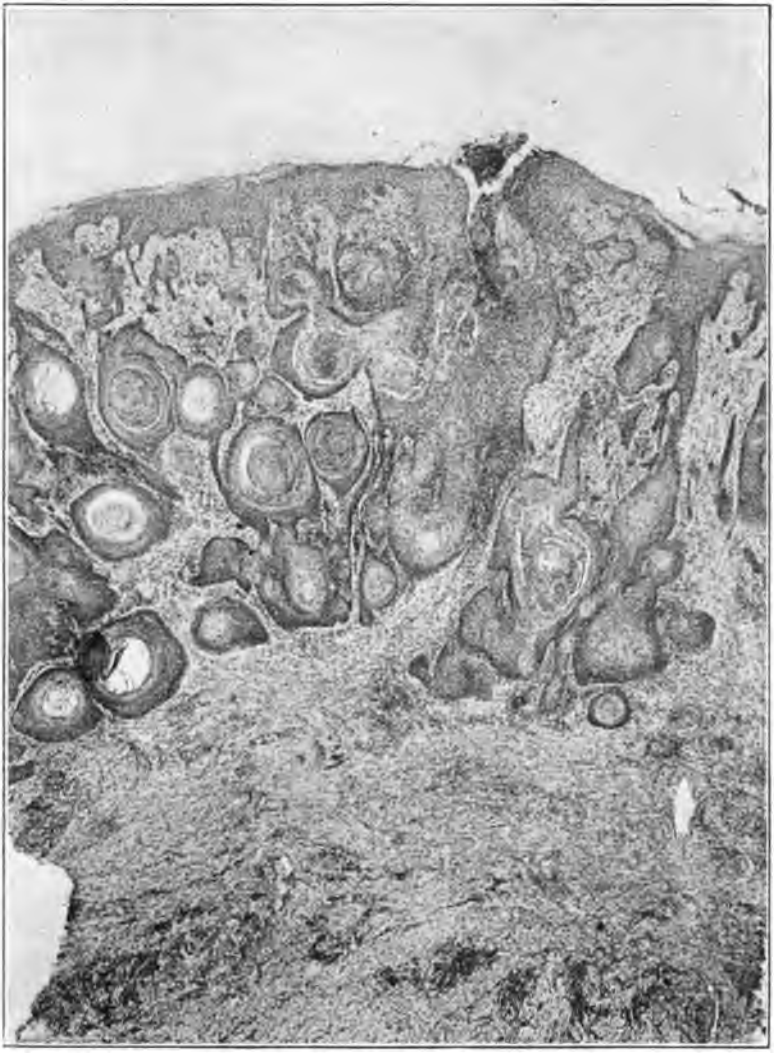

Fig. 8.—Squamous-celled epithelioma (Zeiss Planar 20 mm., C.O.4). An epithelioma which developed in the scar following a burn received 40 years previously. The scar broke down and healed several times during this interval. The slow course of the tumor, which was relatively benign, probably finds its explanation in the cicatricial capsule-like connective tissue resisting the epithelial growth.

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Fig. 9.—Paget's disease. Disease began about nipple two years previously. Condition shows an eroded moist surface, with defined somewhat polycyclic border; nipple retracted. Extending from primary lesion and covering almost entire surface of breast a lymphangitis is present. Over this area were scattered lesions similar to primary one. The mammary gland was the seat of a diffuse carcinoma. Axillary node enlarged.

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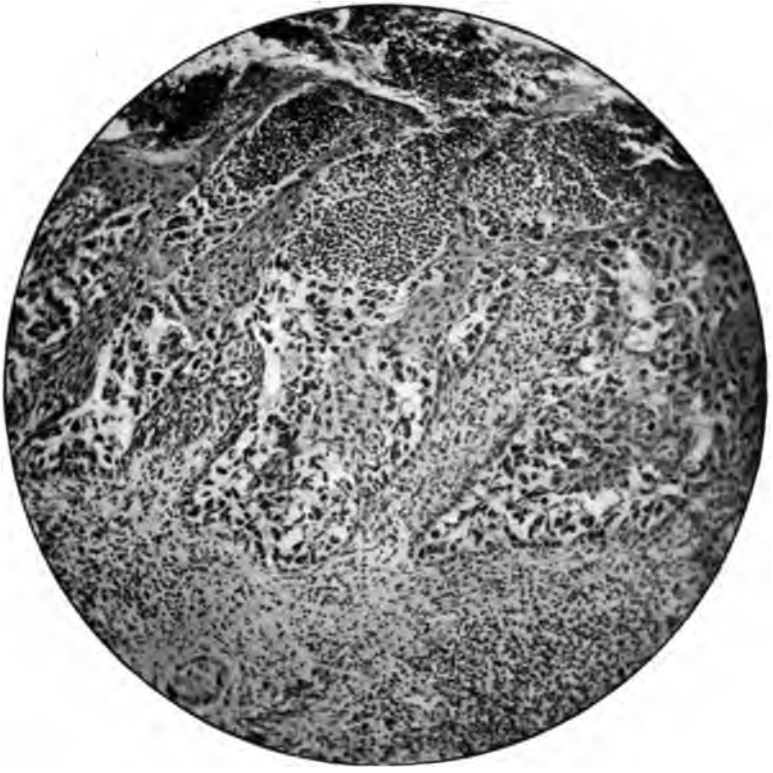

Fig. 10.—Paget's disease of nipple (Zeiss 8 mm., C.O.4). The epidermis shows characteristic change which begins at basal layer and extends to the upper layers, viz., edema, vacuolization and degeneration of protoplasm. At the surface of epidermis is a marked collection of polynuclear leucocytes where erosion has taken place. In the corium cross-section of lymph space showing infarct of tumor cells. Infiltration of lymphocytes, plasma and mast cells in the papillary and subpapillary layers.

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Fig. 11.—Lymphangitis in Paget's disease of nipple (Zeiss 8 mm., C.O.4). Section from erythematous area radiating from disease of nipple. Shows lymph space containing an alveolus of cancer cells.

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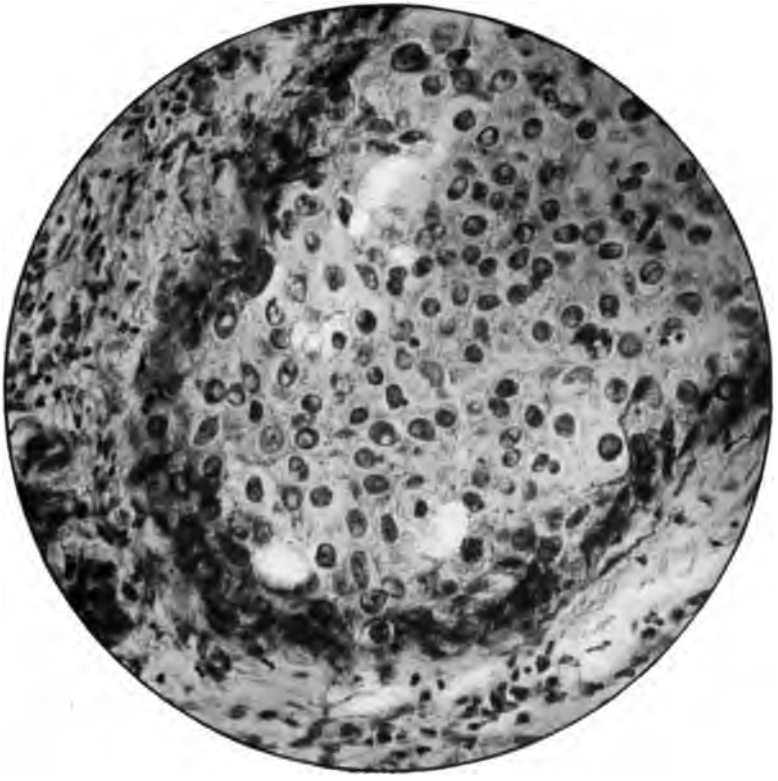

Fig. 12.—Paget's disease (Zeiss 3 mm., N.A.95, C.Q.4). Section through lymphatic infarct, showing cell inclusions.

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called "white-spot disease," as a rule, if not always, is an anomalous localized scleroderma. In certain cases of circumscribed scleroderma the resemblance is striking (Figs. 6 and 7). Here again the initial papule is the important factor. In the case of circumscribed scleroderma above referred to papulation is simulated by the line of cleavage in the skin, but on careful observation the difference can be noted, and in scleroderma involvement of the sweat-pore and pilo-sebaceous follicles is wanting. Finally, in a retrospect of the entire subject the identity of lichen planus sclerosus appears established, but the separate existence of a "white-spot disease" requires further study.

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ETIOLOGY OF CANCER OF THE SKIN

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In the following brief report on cancer of the skin I shall limit myself to a consideration of the epithelial forms of cancer. Even here I shall not be able to go into any detailed discussion and I must ask for indulgence in case I should express my opinions on certain questions without being able to give the data on the basis of which such opinion has been formed.

The etiology of cancer of the skin is, of course, on the whole not different from the etiology of cancer in other parts of the body, and the same principles underlie the formation of cancer in various organs. Cancer of the skin differs from cancer in other parts of the body inasmuch as the pathologic changes taking place in the skin are so much more accessible to direct observation. The clinicians have taken advantage of this circumstance, and to the clinicians we are indebted for some interesting discoveries concerning the causation of cancer of the skin.

EXTERNAL AND INTERNAL FACTORS

In following the origin of cancer of the skin we recognize most clearly the importance of external factors, and to me this is one of the most significant facts. Another conclusion that impressed itself on me in considering the various forms of cancer of the skin is the presence of a second condition which we may designate in a preliminary way as the internal factors.

Now, in the different varieties of cancer of the skin we see these two sets of factors associated in

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various combinations. If the external factor is very potent the internal factors can be dispensed with, and if the internal factors are very potent the external factors play only a subordinate rôle. There are intermediate conditions in which a cooperation of both agencies is of importance. To cite a few examples: In Roentgen ray cancer the external factor alone seems to be sufficient. An internal factor plays apparently a very negligible rôle in this case. It is perhaps similar but not quite as pronounced in the case of the chimney-sweep cancer of the scrotum. On the other hand, in xeroderma pigmentosum the internal factor is very potent and the external factor, although present, is without influence in normal persons of the corresponding age.

It is somewhat similar in persons affected with pigmented moles. The internal factor leading to the production of nevi is of preponderating importance, while in the case of normal people the external factor would be of a very trivial character. In the cancer developing in the skin of the sailors and in old people we are not in a position at the present time to know the relative distribution of the external and internal factors. We lack as yet statistical data sufficiently comprehensive to allow us to state what percentage of persons, in whom the external agency acted with a definite intensity over a certain period of time, became affected. Only on the basis of definite, we might call it, quantitative determintions, could we advance in this direction.

Let us now attempt to analyze those factors somewhat more closely. The external factors[1] of importance are (1) light rays, especially the short-waved and the ultraviolet rays; they play a part in the cancer developing in seamen long exposed to the rays of the sunlight; they determine the lesions in xeroderma pigmentosum, where

1. Interesting observations concerning the action of etiologic agencies have been made in this country, among others, by Hyde (action of light), Hartzell, Schamberg (action of arsenic), Wolbach (effect of Roentgen rays) and Councilman and McGrath (xeroderma pigmentosum).

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the lesions are found in those parts that are more or less exposed to the light. They are in all probability also concerned in the causation of cancer which is found in old people on the basis of keratoma senile, or the so-called seborrheic wart. These changes are mainly found on parts of the body exposed to light. The Roentgen rays are of course responsible for the cancer of Roentgen ray operators. Next, certain chemical factors are undoubtedly the cause of a certain number of cancers. Soot, and especially hard coal soot, causes cancer in chimney-sweeps, and certain chemical products induce cancerous growths in paraffin and coal-tar workers. In these cases the irritating substance, the chemical character of which has not yet been ascertained, attacks the skin directly, reaching it from the outside. In persons taking arsenic over long periods of time this substance influences the skin after having previously been absorbed from the intestinal canal. Mechanical factors are also of importance. There is not doubt that mechanical irritation plays its part in transforming pigmented moles into cancer. And if we include the cancerous affections of the tongue and lip it is certain that the friction of imperfect teeth or the mechanical effect of a pipe may cause cancer. In the latter case heat may perhaps play a certain part, while a combination of heat and mechanical irritation, or either alone, acts in the case of Kangri cancer, observed in Tibet. Here a small stove carried near the skin of the abdomen causes a peculiar cancer of the skin. Among the external factors responsible for cancer we may also mention those conditions or organisms that cause affections, such as lupus, psoriasis, and leucoplakia of the tongue, and various chronic ulcerations and scars, as a sequel of which cancer sometimes develops in the skin and in the tongue. Of course, we must realize that such a sharp differentiation between external and internal conditions does not do full justice to the complexity of nature, and that, e. g., a condition that at one time acted as an external factor may later on

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become transformed into an internal factor and only after such a transformation has taken place it may act as a cause of cancer. And this is what some pathologists, indeed, assume to take place. A distinction between conditions outside the organism, conditions inside the organism but outside the epithelium and conditions inside the epithelium would be more correct.

In regard to the internal conditions our knowledge is much less definite. We know that melanotic cancer frequently starts from a pigmented mole and that the latter is a condition present at the time of birth or developing in very early life, and probably due to developmental abnormalities which may be hereditary. A certain localized congenital and also hereditary condition is therefore one of the internal factors leading to cancer.

In xeroderma pigmentosum some internal factor making the skin peculiarly susceptible to the action of light and ultraviolet rays is undoubtedly present. In the absence of positive knowledge we may propose the following hypothesis: We know that certain substances, especially fluorescent stains, are able to sensitize living cells as well as ferments to the injurious action of light. We furthermore know that cattle that feed on buckwheat (*Buchweizen*) become very sensitive to the influence of light rays, and skin affections follow if the cattle are exposed to the light. It is possible that in xeroderma pigmentosum a substance is produced internally that sensitizes the skin and certain mucous membranes to the action of light; the last stage of the light action in a sensitized skin is the development of cancer. Whether primary differences in the anatomic structure of the skin and mucous membranes are present in patients affected by xeroderma pigmentosum has to my knowledge never been examined. Nor is anything known, so far as I am aware, in regard to the sensitiveness of the skin in such patients toward the action of other than light and ultraviolet rays. Whatever the ultimate character of this internal factor is, it must in some cases have been indi-

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rectly transmitted through the germ cells of the parents, probably in the form of a preparatory substance, inasmuch as it is known to occur in sisters or brothers of the same family. Nothing definite is known concerning the existence of internal factors in the cancers of old age, cancer after use of arsenic, cancer in chimney-sweeps and other similar conditions. We might be inclined to believe in the presence of some predisposing internal factors in such cases inasmuch as we notice that only certain persons are affected by cancer or seem, at least, to become affected much more readily among a much greater number of people exposed to the same injurious influence. We must, however, be well aware of the fact that in such cases we cannot be certain that the same quantity of external injury, if we may thus express it, acted on all the persons exposed.

EMBRYONIC THEORY

There are other internal factors to which a great or, we may say, the almost sole responsibility has been attributed. I refer especially here to the views expressed by Borrmann. This author made extensive microscopic studies of early stages of carcinomata of the skin, and came to the conclusion that cancer of the skin is in almost all cases due to embryonic malformation which leads to complete separation of certain parts of the epithelium from the rest of the epidermis and their transposition into the corium. Thus the corium carcinomata are produced which include, for instance, the cases of rodent ulcer. Or certain parts in the epidermis may remain in an undifferentiated condition and give rise later to the prickle-cell, keratinizing carcinomata, according to Borrmann.

It is impossible here to go into a detailed criticism of his observations and deductions. Suffice it to say that the results of histologic examinations of others, among whom I might mention H. H. Janeway, do not uphold his view. The typical carcinoma of the skin originates

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through a direct downgrowth of the surface epithelium or its appendages, and all the evidence at hand proves that, although perhaps in a few cases, carcinoma may take its origin in misplaced embryonal rests, embryonal displacements are of no or of very slight importance in the etiology of the large majority of the cancers of the skin.

RIBBERT'S THEORY AND THE CANCER CELL

In the last analysis Borrmann's views are based on the hypothetical conceptions of Ribbert, and, inasmuch as the views of this author had a dominating influence, at least for a certain period of time, we must briefly refer to the latter. In the course of time Ribbert changed his views considerably, so that at present little is left of what characterized his original conceptions. But the distinctive feature of his hypothesis was the following:

The carcinoma cell in its last analysis is nothing but an ordinary regenerating epithelial cell, such as is seen in wound healing. The only difference between cancerous and ordinary regenerative growth is to be sought in some secondary conditions which do not permit the epithelial cell to unite with its kin to form again a normal organ. In most cases the presence of the inflamed connective tissue is responsible for the separation of certain parts of the epithelium. This is the principal conception of Ribbert's theory, and the facts do not sustain it. The carcinoma cell is not an ordinary regenerating cell. The latter may be put into whatever environment we choose; it always follows the laws that are valid in the case of regeneration. The carcinoma cells remain carcinoma cells even if on both sides they are surrounded by its kin, the normal epithelium, or wherever they may be implanted. Indeed, the transformation of an epithelial into a carcinoma cell takes place, in many cases at least, at a time when the epithelial cell is still in union with the surrounding epithelial tissue. All the experimental evidence at our disposal admits of but this conclusion.

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Epithelium may grow in agar or blood-serum in the body or in intimate contact with connective tissue and the blood-vessels; the epithelial cells do not behave like carcinomatous cells; on the other hand, we may transplant carcinomatous cells and they will always grow as carcinomatous cells, if growth can be obtained.

This invariable difference between ordinary epithelial and carcinomatous cells induced some writers to seek for a preformed internal factor in the congenital constitution of the cell, and especially of their chromatin. This view appears to be as little justified as the opinion that as a rule cancers of the skin are due to embryonal misplacements. Nor would I recommend at the present state of our investigations the designation of carcinomatous cells as "new cell races" or the use of the term "anaplasia." I believe that all such terms are unnecessary, and that they frequently tend to obscure the real problems which consist in determining functional relations.

AGE AS A FACTOR

There remains another condition which might be classed among the internal factors, and on which great stress has been laid by various writers, namely, old age.

It is certainly correct to state that carcinoma occurs more frequently in advanced age and that certain cancers of the skin are especially found in the senile skin. If, however, we analyze more searchingly what is called old age in the case of its epidermis we will find that we have to deal with a complexity of factors, among which external injurious influences play directly or indirectly the most prominent rôle. The commonly assumed basis for old age is the conception of a certain deterioration in the machinery of the cell which is necessary to occur in the course of time and which is inherent in its structure. As I pointed out nine years ago, I believe this view to be erroneous, especially as far as the cells of the epidermis are concerned. There are weighty reasons why we should believe in the potential immortality of the epidermal

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cells rather than in their necessary aging. If the senile changes take place in the epidermis they are according to this view due to a long-continued cumulative action of injurious external agencies, as light, heat, mechanical insults, and so on, which acted either directly on the epithelial cells or on the stroma on which the latter live; injurious influences which made themselves felt continuously and from the effects of which no recovery was therefore possible. As far as the epidermis is concerned, old age is therefore a term designating the effects of long-continued external injurious factors. Instead of explaining various skin lesions as due to a premature senescence of the skin we should, it appears to me, take the opposite position and explain the senile changes of the skin as due to the action of injurious external influences.

MICRO-ORGANISMS

By what mechanisms do the external factors which have been enumerated affect the epidermis and how can they call forth a cancerous proliferation? In the first place we might think of the activity of micro-organisms that have an intracellular existence and are therefore constantly acting on the epithelial cells, stimulating them to active cell division and to invasion into the neighboring tissue, such stimulation being to some extent accompanied by changes in cell metabolism calling forth new enzymatic activities. We know, indeed, that certain micro-organisms as those of variola and vaccine and molluscum contagiosum call forth epithelial cell proliferation, and Borrell designated such a condition under the term epitheliosis in contradistinction to epithelioma. And there exist observations made in the course of the experimental investigation of cancer which could be readily explained by the assumption that micro-organisms have an etiologic significance. On this basis all the changes induced by the various external and internal conditions which we mentioned would only serve as means of introducing a certain micro-organism into the

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epidermis. Although at the present time we cannot deny, and although we must keep in mind such a possibility, we must confess that the probabilities of such a connection between external agencies and cancer appear exceedingly slight at the presenet time. No tangible indication of micro-organisms that withstood the test of later investigators could be found.

IRRITANTS

On the other hand, we see before us the prospect of an ultimate understanding of the connection of external irritants with cancer by a more penetrating analysis of the biology of the various tissues, and especially will it be necessary to inquire into the influence which external agencies have on growth processes. Concerning the action of Roentgen rays and radium, considerable stress has been laid on their necrotizing effect. But especially, recent studies have shown that, independently of their necrotizing action, these radiations have a distinctly stimulating effect on the epithelial cells; we furthermore learned that under the localized influence of certain organic derivatives, especially aromatic amido derivatives a limited infiltrative growth of epithelium into the deeper connective tissue structures may take place. It was mentioned above that a combined action of internal and external factors caused carcinomatous growth in certain, probably in many, cases. Recently some advance has been made in the experimental analysis of formative stimuli which throws some light on such a combination of factors and makes it amenable to a quantitative analysis. It has been found that a substance produced by one organ of the body unites with the connective tissue cells of another organ, and that if such a combination has taken place mechanical stimuli can cause an extraordinary, though temporary, tumor-like tissue proliferation. In this case the chemical activity of an organ of the body represents the internal condition and the mechanical irritation the external agency. Such

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experimental means and studies will allow us to eliminate many variable factors which complicate the development of natural tumors. Although these experimental products which have just been mentioned differ from tumors, mainly in not being permanent, they nevertheless will throw much light on the conditions on which exuberant growth and infiltration of surrounding tissues depend, and will thus help to clear up the mechanism of cancerous growth.

ANATOMIC CHANGES

To this physiologic point of view of considering phenomena of abnormal growth may be opposed the anatomic point of view which undertakes to explain functional changes, such as variations of growth-energy as represented by tumor growth, on the basis of histologic appearances of tumors.

Thus in many changes in the skin due to long-continued external irritation we find a more or less a similar sequence of anatomical changes. These typical anatomic changes have been termed "precancerous conditions." Cancers which are caused by the action of light and ultraviolet rays, and also by Roentgen rays and arsenic, and those found in senile skin, are preceded by hyperemia, pigment formation in the epithelial and pigment deposit in cutis cells; increase in the proliferation of epithelial cells, sometimes combined with the formation of epithelial giant cells; hyperkeratinization, formation of warts, and at last cancer formation. In certain conditions (e. g., xeroderma pigmentosum) the hypertrophic processes in certain parts of the skin may be accompanied by atrophic processes at other places. In the later stages certain parts of the connective tissue show definite changes; they become hyaline while other parts directly underneath the epidermis may show a rarefication. Many blood-vessels may be obliterated.

Now various writers attributed to these changes as such an etiologic significance in the development of can-

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cer. Thus Unna ascribed to the overproduction of pigment some importance; a very improbable assumption, if we consider that on the whole colored races are less liable to cancer of the skin. The production of melanin in the skin depends in all probability on the activity of certain oxydative ferments, and it is conceivable that under stimulating conditions, among other changes, a correlated change in certain oxydative processes in the cells may take place. Others held hyperkeratinization, as such, responsible; again a very unlikely assumption. Hyperkeratinization being merely the expression of atypical growth phenomena which are taking place in the skin, cannot be considered as the cause of these growth processes. Others accused the obliteration of blood-vessels; this condition, it was argued, forced the epithelial cells to obtain their food-supply from connective tissue cells; which latter process was said to act in a similar manner as the penetration of a spermatozoon into the ovum, a somewhat fantastic comparison with hardly any foundation of fact. Ribbert believed in the etiologic importance of a subepithelial cell-infiltration. But this is not always present at the commencement of the cancerous growth. Others assume that the chronic connective tissue changes liberate the latent energy of the epidermis. It is, however, difficult to see why very dense connective tissue should, as such, be favorable to epithelial growth. In all probability it would prove to be very resistant to the expansion of the epithelium. In many cases of cancer of the skin, moreover, no such connective tissue changes are present. Unna, for instance, especially noticed their absence in certain cases of sailor's skin cancer. On the whole, it is therefore more probable that epithelial proliferation and connective tissue changes are coordinate and that the latter are not to be considered as primary processes. In a few cases it was noticed, first, it seems, by Roessle and Spude, and recently also by Janeway,

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that in the early stages of cancer the epithelium grows down in the direction of dilated blood-vessels and in some way or other the presence of such dilated blood-vessels was held responsible for the development of cancer, without, however, any convincing reason being given for the validity of such an explanation. In many cases, moreover, such a relation between dilated vessels and epithelial proliferation is absent. We must realize fully the great difficulty in explaining functional phenomena on the basis of certain histologic appearances, however, frequently the latter may be found. There are many variable factors present in such phenomena and the chances are so great that only indirect connections exist between a certain histologic picture and the functional condition it is called for to explain, that it is not safe to use it as the basis of a more or less elaborate hypothesis.

CONCLUSION

Through experiment alone we can eliminate the variable factors one after another, and slow as the experimental procedure may appear, it will ultimately prove to be the only safe guide in our work. I do not, however, underestimate the value of histologic investigations, which in many other directions have proved to be of inestimable value, and which are also necessary as an adjunct in the etiologic study of cancer, but in the latter only in a subsidiary way. Until further experimental investigations shall enable us to discriminate with greater accuracy between the various factors and their mode of action, one must be content to state that in many cases of cancer long continued external irritation is of the greatest etiologic significance; that long-continued stimulation of the epidermis may lead to the formation of cancer; that it is, however, at the present time not possible to state how much of this stimulation is exerted directly on the epithelial cells through the external agency, and how much is an indirect effect

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caused by changes in the organism as a whole or in the underlying connective tissue. But even if these latter changes should prove to be of greater significance, and not to be merely coordinated changes, they must be assumed to stimulate by physicochemical processes the overlying epidermis. Until we know more of the more distant effects which long-continued external stimulation may exert on cells, and which may find expression only after a very protracted period of latency, we must beware of too detailed explanations. We can, however, be certain that as the result of long continued irritation the epithelium changes in its proliferative power and that such changes are transmitted to the following cell generations apparently indefinitely.

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THE PATHOLOGY OF MALIGNANT EPITHELIAL GROWTHS OF THE SKIN

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The presentation of this subject as a lantern exhibition permits the demonstration of a large number of slides showing the usual and unusual features of the two main types of cutaneous epitheliomata and some of the conditions which precede their growth. As it is obviously impossible to reproduce all, either pictorially or graphically, in a paper of this scope, only a few selected ones will be introduced to emphasize certain features, and in the text reference will be made to those of interest which have been published elsewhere.

PATHOLOGY

There is perhaps no field in tumor pathology which offers such facilities for the study of diversity in histologic structure as the growths of the skin, nor one which furnishes the opportunity for investigating such a variety of mediate causes. In the vast majority of cases a tumor when first seen is beyond its first inception, malignancy is already established, and its genesis and initial changes left to speculation. In the skin, however, owing to the ease with which changes can be noted, and the slower rate of growth, it is possible frequently to obtain material which shows early transitional stages. In addition, we have a group of conditions which are so definitely associated with tumor formation that on a clinical basis alone we do not hesitate to prognosticate

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their outcome. These affections, classfied as precancerous and highly important from a dermatological standpoint, permit us not only to draw deductions as to the etiologic and biologic factors concerned in malignant proliferation, but they confirm the view that a plurality of causes is operative in the etiology of cancer. While admitting the contention of Borrmann and other adherents of the Cohnheim theory, that in certain cases tumors have their origin in embryonal cell rests, as in those springing from certain nevi, the weight of evidence in the majority of cutaneous epitheliomata is not in favor of this view. In the examination of early growths, especially the superficial epitheliomata which arise on a seborrheic base, single or multiple foci of proliferation can be seen proceeding directly from the epidermis. These areas are usually sharply delimited from the surrounding surface and appear as swellings bulging toward the corium. The cells are smaller, more closely and less regularly placed than normally and the basal layer has lost its symmetry. They are, furthermore, to be distinguished from the surrounding cells by their larger and deeper staining nuclei. In some of the superficial epitheliomata of the Paget type edema of the affected area is the characteristic early change; the cells increase in volume and their pale bodies stand out in sharp contrast with the neighboring normal ones.[1] Findings like these and the evidence offered by the precancerous class of diseases it seems to me negative the view which incriminates isolated cell groups, in the skin at least.

ETIOLOGIC FACTORS

The epidermis is susceptible to stimulation by a variety of influences. This is seen in the large number of dermatologic affections which are accompanied by abnormal proliferation of the epithelium. In the majority of these the proliferation remains within the bounds of an

1. Paget's Disease of the Gluteal Region, Jour. Cutan. Dis., 1905, xxiii, 193.

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inflammatory process, but not at all infrequently malignancy intervenes. What is the factor that gives rise to the initial impulse? By the investigators interested in this subject it is believed that this impulse is stored up in the nucleus. So long as a cell is engaged in the performance of its function it uses up its energy and cannot at the same time conserve energy for proliferation (Adami) but with a disturbance of function conditions are changed and the vegetative powers of the cell gain the ascendant.

Recapitulating briefly some of the factors which stimulate epidermic cells, micro-organisms like the staphylococcus, or its toxins, may produce such an overgrowth that large areas of skin, as of an entire extremity, are converted into a fungating mass. This is sometimes met with in dermatitis vegetans. In tuberculosis verrucosa, in which the tubercle bacillus gains entrance through the skin, the tissue is excited to warty hyperplasia whereas in the other forms of cutaneous tuberculosis the epidermis is but little altered. In yaws the spirochæta pertenuis, which is constantly found between the epithelial cells, produces a lesion consisting of marked epithelial hyperplasia, which gives the disease its peculiar characteristics. In syphilis, leucoplakia and condylomata are striking examples of epidermic proliferation. The enormous fungations accompanying blastomycosis are probably the result of the reaction of the epidermis to the blastomycetes, that being their portal of entry. Molluscum contagiosum, common warts, and Darier's disease are further illustrations of acanthosis; although the nature of the respective stimuli is not determined.

Chemical substances like tar and paraffin, arsenic, tobacco, scarlet red, etc., likewise possess the power to excite epithelial growth. From tar and its derivatives we may have all grades from a mild stimulation leading only to overgrowth of the horny tissue, as in the acne lesions, to multiple malignant tumors. Between these

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stages may be seen the development on telangiectatic patches of flat warts in which malignant transformation takes place.

As a result of the prolonged administration of arsenic, certain changes are brought about in the skin which result in pigmentation, scaly patches and warts or keratoses, with epithelioma as a sequel. The injection of various substances in the skin of animals has been followed by epitheliomatous development, as shown by the experiments of Fischer and Stober with scarlet R. Indol, skatol and other products of intestinal fermentation injected into the ear of a rabbit by Stoker and Wacker also brought about a reaction indistinguishable from carcinoma.

Of the physical agents, light is one of the most important factors in its power to induce certain changes in the skin which lead to epithelial proliferation. We are largely indebted to biologic research for our knowledge of the potency of this energy and its good and evil effects. From investigation on the elementary forms of life it has been ascertained that the properties of the protoplasm of these organisms may be completely modified by the action of light energy, causing them to assume new forms and even so change the conditions of existence that an aerobic organism may become anaerobic under its influence. From his observations on the heliotropism of plants, Sachs formulated the law that light of constant intensity acts continuously as a source of stimulation. A heliotropic action on the part of animals in accordance with that observed by Sachs was also demonstrated by Jaques Loeb.[2] The effect of light on the normal skin is an erythema, acanthosis and thickening of the corneous layer. Its relation in the production of pigment is too well-known to claim more than passing mention. It has, further, been demonstrated that it is the short waves—the blue and ultra-violet rays—which constitute the pernicious element in the

2. Cleaves: Light Energy, 1904.

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production of pathologic conditions. These actinic rays acting on a senile skin, or that of persons exposed to the weather, as sailors, are capable of producing such changes as telangiectases, pigmentations, atrophic lesions and warts, one or more of which may become malignant. The telangiectatic and pigmented lesions are the processes of defense on the part of the organism to protect itself against their injurious effect. Difference in susceptibility is a matter of every day observation. This is seen in the freckling of a supersensitive skin and in the way different people react to sun-burn, it being mild in one case and intense in another. In xeroderma pigmentosum changes are found identical with those met with in the senile skin, light exciting the same syndrome of symptoms as in the aged. The primary condition is a congenital defect of the skin either local or due to some internal cause (Loeb) which renders the integument vulnerable to the action of light and brings about in it a precocious senescence. *X*-ray in its effects is similar to solar light. On the normal skin its action is to interfere with secretion and the function of the cells, and if prolonged it results in degeneration and destruction, finally leading to new growth.

Observation of facts like these favor the view that the essential stimulation to epithelial growth may be multiple, in one degree leading to a limited increase of cells and in another to lawless growth, the amount of stimulation or the susceptibility of the individual determining the result. The study of the sections of pre-epitheliomatous changes in the cell would favor the view that it is in the cell nucleus that the first effects are produced, probably in the chromatin loops, which possess vegetative and specific function, as suggested by Oertel. With the loss of the essential secreting function there is an exaggeration of the vegetative power. In the breast, for example, when the capacity to secrete milk is suppressed the cells may become vegetative and proliferate, although this may happen in the active stage of the gland. Similarly

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in the liver and stomach when functional activity is interfered with the vegetative properties of the cells preponderate.

Skin cancers afford much evidence that they start from degenerated cells, as in leucoplakias, keratoses, degenerations brought about by light, solar and *x*-ray, chronic inflammatory processes, etc. Many of our dermatologic observations, therefore, fit in with Oertel's theory as we may see cells proliferate in close proximity to degenerated ones.

PRECANCEROUS AFFECTIONS

Of the precancerous conditions senile keratosis comes first in order of frequency. Its sites of predilection are the face, neck, and backs of the hands, the parts of the body exposed to the influence of light. It is not infrequently accompanied by seborrhea of the face and scalp, so that it is difficult to know just how much weight to attribute to the infection of the epidermis and how much to the influence of light. The various stages of its development are frequently seen coincidently. The first noticeable change is the brownish discoloration of the skin. This is followed by a slight thickening of the epithelial cells and practically corresponds to the seborrheic wart. As the lesion develops it increases in depth, its warty character becomes more pronounced and it is in this stage that we have virtually an epithelioma. These lesions differ from the ordinary verrucæ in that they are more pigmented and less elevated, and in their later stages they are covered by a greasy friable crust which is not so adherent as the epidermic layers of the ordinary wart. It can be detached with little effort and then reveals a bleeding papillomatous condition. At this stage the lesion can be readily removed by curettage and caustics and heals with the production of a slight scar. Not infrequently in the same individual we can see lesions in all stages of development—the telangiectases, brownish or blackish discolorations not appreciably

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raised above the surface, flat seborrheic warts and those showing considerable elevation, with the adherent crust above referred to.

ILLUSTRATIVE CASES

Figure 1 illustrates a patch of keratosis from the cheek of a man 60 years old. In addition to numerous pigmented, telangiectatic and keratotic lesions on his face and hands, he had three active squamous-celled cancers, one over the bridge of his nose, another under his left eye and the third over the left parotid region. The lesion from the cheek shows a thickened horny layer which was somewhat broken up at the time of biopsy and is separated into strata by extravasated blood. The nuclei are fairly well preserved; attached to its under layers are cornified plugs which distend the mouths of the pilosebaceous apparatus. The granular layer is missing. The rete is irregularly thickened and thinned and has areas of degeneration which stain badly and contain vacuoles. On the whole the cells are smaller than normal and the sharp contour of the basal layer is lost. The small areas of cells which are closely crowded and stain more deeply than the surrounding ones are probably part of the follicular appendages. The connective tissue in the upper corium is degenerated, its fibrillary character is lost and it has acquired a homogeneous appearance. The majority of the vessels have very thick walls and small lumina. A mild inflammatory infiltration is present in the superficial part of the cutis.

The senile keratoma, shown in Figure 2, was removed from a patient 47 years old, who presented a squamous-celled epithelioma of the index finger, several warty growths on the backs of his hands, as well as telangiectases, atrophic and pigmented lesions. Under the low power there is a striking resemblance between this wart and those seen in xeroderma pigmentosum. The higher power (Fig. 2) shows principally the degenerative changes in the cells. From hyalin and hydropic changes they have become voluminous, lost their prickles and assumed a more or less rounded form with a well-defined periphery, as though encapsulated. In the older portions they have become confluent and their outlines are no longer visible. The nuclei in many have entirely disappeared or only shrunken bits of chromatin remain surrounded by a clear space, or are connected with the cell by radiating protoplasmic threads. In addition free cells are found appearing as spheres of hyalin with a dense nucleus and a vacuole. The connective tissue beneath the wart, and especially on either side of it, is degenerated and rarified. It is this rarification of the subepithelial tissue which Thiersch considered the necessary or determining element in tumor

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growth. By bringing about a disturbance in tissue tension the restraint to epithelial invasion is removed.

Figures 3 and 4, examples of xeroderma pigmentosum, are from the tissue of a young man, aged 21, with the typical features of the disease developed on his face, neck, hands and lower portions of the forearms. He also had a well-advanced epithelioma of the lip. Figure 3 shows one of the smaller keratotic lesions. The horny layer is markedly thickened, very dense and firmly adherent below. The granular layer is absent. The rete is very irregular, consisting in places of only two or three layers of stretched cells and in others of irregular processes, whose cells vary in shape and size, but have atrophic bodies and conspicuously large nuclei. The prickles are not distinguishable as the cells are more or less welded together. Hyalin degeneration is a marked feature. The basal layer is in a state of disorganization, with the tissue immediately below it vacuolated. The corium is atrophic and degenerated; the papillary and subpapillary regions are occupied by a dense infiltration of lymphocytes and plasma cells.

The larger warty growth (Fig. 4) also shows a dense horny layer. The epithelium below is irregularly proliferated and composed of small atrophic cells, with, in the central portion of the lesion, hyalin degeneration and pearl formation. Many nuclear figures and atypical mitoses complete the histologic picture of these growths. The changes in the corium are similar to those in Figure 3.

Figure 5, illustrates telangiectases. The tissue is from a patch of dilated capillaries which followed an x-ray burn. The horny layer is considerably thickened, the rate flattened and hollowed out by the dilated capillaries. The cells are smaller than normal and many of them contain vacuoles. The papillary bodies have been entirely obliterated and the corium changed by hyalin degeneration. The tortuous ectatic capillaries extend from the middle two-thirds of the cutis to almost beneath the horny layer. Some of the sections contain partial thrombi.

Arsenical keratosis, (Fig. 6). This tissue came from a patient kindly referred to me by Dr. Jackson. He had taken Fowler's solution for five years. On his body and hands were numerous scaling, pigmented and warty lesions. The section from one of the keratotic areas shows the thickened horny layer dipping down into the rete, producing a marked undulatory line between the two. In some of the layers the nuclei are well preserved; in others as the result of dyskeratosis there are large ballooned bodies which appear like double-contoured organisms. The granular layer has almost entirely disappeared, the horny layer proceeding directly from the Malpighian layer.

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In the latter the points of interest are acanthosis and edema, causing a widening of the intercellular spaces. Here and there the cells have disintegrated, their remains lying in cystic spaces or several have fused to produce large, deeply-staining, irregular bodies connected by cytoplasmic threads to the surrounding cells. Nuclear degeneration is as common as cytoplasmic. Some of the cells contain central clumps of chromatin; in others it is dispersed through the cell, and a further sign of degeneration is the presence of clumped nuclei, due probably to amitotic division. The basal layer is disorganized at points where the corium is more or less rarified. The superficial part of the cutis has a granular appearance and the connective tissue celle stain only faintly. Aside from this a slight lymphocytic infiltration is seen about some of the capillaries.

Leucokeratosis produced by syphilis or tobacco, or occurring independently of either, is probably the most common antecedent change in mucous membrane epitheliomata of the mouth.[3]

In addition to the foregoing which represent a group of conditions whose natural history includes a termination in epitheliomatous formation, there is another class of diseases which offer a favorable base for the development of malignancy. They are chronic skin diseases, as syphilis, lupus vulgaris, lupus erythematosus. Darier's disease, psoriasis, scars from various causes, etc.

Cancers secondary to tuberculous lupus are in the majority of cases, classed as scar cancers or are attributed to the use of *x*-ray in treatment. However, they also develop, on an active lupus and are usually of the squamous-celled variety, in which cases both processes appear co-incidentally under the microscope.

The accompanying case is of peculiar interest, in its departure from the usual type seen in connection with tuberculosis or scars. It was originally reported as an endothelioma,[4] but a greater familiarity with the basal-celled growths and their degenerations has led me to include it in the latter group. The tumor, which developed in a lupus scar, occupied the entire corium as large and small cellular masses, irregu-

3. For a description of the character of these lesions the reader is referred to Affections of the Mucous Membranes and their Relation to Skin Diseases, Jour. Cutan. Dis., 1904, xxii, 397.

4. Am. Jour. Med. Sc., August, 1900.

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larly rounded, oval or elongate (Fig. 7). The cells, many of which are spindle-shaped from pressure, have rather large oval nuclei, rich in chromatin and contain numerous mitotic figures. The central portions of the cell masses from degeneration are cystic and contain detached cells and detritus. There is no connection anywhere with the surface epithelium, and no evidence of the tuberculous process is present.

In a case of epithelioma following a burn, which was previously reported,[5] the tumor developed on a chronic ulcer of the thigh following a burn received forty years previously. The ulcer healed and broke down several times, eventually passing into neoplastic formation. The slow development probably finds its explanation in the histologic structure (Fig. 8), which shows the sharp limitation of the growth by the underlying sclerotic tissue, which, capsule-like, retarded the epithelial invasion.

The co-existence of epithelioma and psoriatic patches is a rare occurrence, but through the kindness of Dr. Dr. George T. Jackson I had an opportunity of seeing such a case several years ago. Multiple tumors of the basal-celled type were present. The patient subsequently developed metastases in the mediastinal glands and internal organs and died of carcinosis. The tumors were made up of masses of small, deeply-staining cells with scant stroma and numerous foci of degeneration of a mucinous character in the cellular aggregations.

The slides demonstrating epithelioma and Darier's disease were made from specimens kindly loaned me by Dr. Grover W. Wende from his case of multiple squamous-celled epitheliomata consecutive to Darier's disease. The interesting feature in connection with these growths was the degenerative forms and cell inclusions.

The subject of malignant growths secondary to nevi, with illustrations, has been previously discussed by me.[5, 6]

Paget's disease of the nipple is regarded by many authors as a superficial epithelioma, and this view is probably justifiable on clinical grounds, since we find

5. Some of the More Unusual Forms of Epithelial Growths of the Skin, THE JOURNAL A. M. A., Oct. 24, 1908, p. 1399.

6. Melanomas and Some Types of Sarcoma of the Skin, THE JOURNAL A. M. A., Jan. 8, 1910, p. 91.

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Fig. 13.—Squamous-celled epithelioma (Zeiss 8 mm., C.O.4). Showing downgrowth from the surface epithelium and alveoli with pearl formation.

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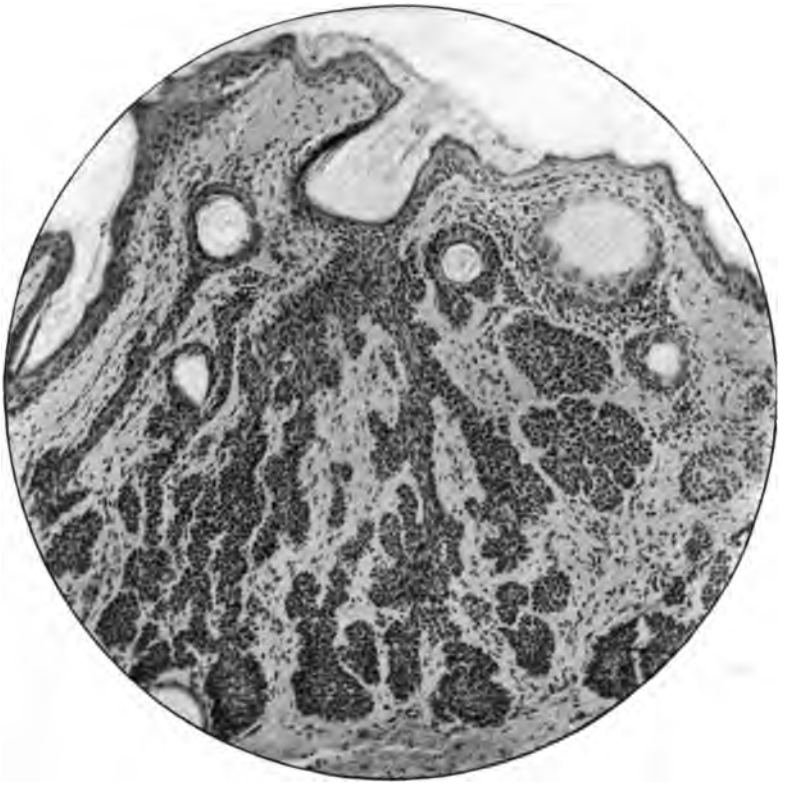

Fig. 14.—Rodent ulcer (Zeiss 8 mm., C.O.4). An early rodent ulcer near ala of nose, taking its origin from the lanugo hair follicles.

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Fig. 15.—Basal-celled epithelioma (Zeiss 8 mm., C.O.4). Rodent ulcer, side of nose. Sharp line of demarcation between tumor growth and epidermis. Marked mucinous degeneration of tumor, resulting in certain areas in cystic cavities.

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Fig. 16.—Multiple epitheliomata. Woman, aged 60, with multiple superficial flat and fungating epitheliomata.

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in other portions of the body superficial flat epitheliomata having an eroded granular center and a slightly rolled polycyclic margin, strongly resembling the nipple lesion. Histologically, however, some points of difference are to be noted, especially in the older portions of the extra-mammary cases. If the edge of these lesions is examined, the picture in many instances bears a very close resemblance to the mammary disease. The cells are edematous, vacuolated, and show the peculiar degenerative changes of the affection. There is, however, evidence of proliferation, and if the central portion of the area is examined, true epitheliomatous formation of the small basal-celled type will be found.[1, 5] In the nipple region while there is a marked acanthosis of the epidermis the line of demarcation between epidemis and corium is preserved, and in a series of cases that I have examined downgrowth did not occur. In these cases there was concomitantly a mammary carcinoma and the corium was infiltrated solely with growth from the lactiferous ducts below.

The photograph (Fig. 9) is from a Russian woman about 55 years of age, referred to me by Dr. Keene. The patient stated that the condition of the left breast had existed about two years. It presented the typical features of Paget's disease, a dark red, granular, exuding surface with sharply defined periphery, with here and there evidence of beginning cicatrization in the center of the lesion. She also presented a group of small secondary ulcerated and encrusted lesions outside of the original patch. These lesions suggested autoinoculation or the breaking down of a lymphangitis, which radiated for a distance of about three inches from the periphery of the patch. The entire breast was the seat of a carcinomatous tumor, which was not sharply circumscribed, but seemed to involve the entire gland, probably due to the simultaneous infection of the lactiferous ducts. She also had an enlarged node in the axilla.

Tissue from the nipple region (Fig. 10) shows the epidermis riddled, as it were, by some destructive agent. The process has proceeded to complete autolysis in some areas, or only distorted nuclei and fragments of the cell body remain. The surface of the epidermis is eroded and covered by a crust of polynuclear leucocytes, remains of epidermic cells and fibrin, and below this there are miliary collections of leucocytes.

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The specific degeneration in Paget's disease begins in the deepest layers of the rete and causes the cells to become paler and increase in volume. From swelling the prickles become indistinct or disappear entirely and vacuoles make their appearance. In this way there may comes to be left only a ring of protoplasm separated from the nucleus by a clear space, or the latter may be distorted or pushed aside by one or more vacuoles. Eventually the cells are separated and lie free in cavities and assume most bizarre forms and appearances. The basal layer, although degenerated, still sharply marginates the epidermis from the corium. In the cutis, with the beginning epidermic changes, an infiltration of mast and plasma cells appears in the papillæ, later becoming more diffuse and extending to the subpapillary layer and the tissue below. In the case under consideration the superficial lymphatics contained cancerous infarcts.

The histologic findings from the area of lymphangitis are shown in Figure 11. The tissue immediately about the cancer embolus is denser than elsewhere, owing to the reactive fibrosis which has taken place. The cells are large, irregular and show pronounced degenerative changes (Fig. 12). Their protoplasm is coarsely granular, and in going through the sections seriatim all types of so-called cancer bodies, dependent on cellular and nuclear origin and aberrant mitosis, are to be met with.

These curious changes are, however, not peculiar to malignant growths but are also found in chronic inflammations, and irregular mitotic figures have been produced experimentally in various tissues. Degenerating cells may also divide by amitosis, giving rise to a clumping of nuclei.

Illustrations and report of lymphangitis in cancer en cuirasse will be found in my paper already referred to.[5]

CLASSIFICATION

Cutaneous carcinomata in the great majority of cases take their point of origin from the epidermic covering of the sheath of the follicles, the glandular epithelium only exceptionally proliferating primarily. Although

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there are many classifications based on the microscopic or macroscopic appearances, relative malignancy or genesis, the histologic division of cutaneous epitheliomata into two great groups, according to certain prominent characteristics is the most practical, namely, the prickle-cell group, and the basal-cell group of Krompecher. In the former, the tumors are composed of large cells which have retained their prickles; they are early destructive, metastasize and have a general malignancy. In the basal-celled group the tumors are made up of small cells which possess no prickles and have relatively large nuclei; they do not as a rule metastasize and have usually only a local malignancy. While recognizing the validity of the criticism made by Adami that all cells originate from the basal layer, it is nevertheless a fact that in the one case only one type of cell continues to proliferate while in the other differentiation goes on. As a rule, too, these two types conform more or less with distinct clinical pictures, though occasionally cases are seen in which a positive diagnosis can only be made by the microscope. Patients with multiple epitheliomata sometimes present the two types with not sufficient clinical difference to tell them apart.

Histologically the typical feature of squamous-celled growths is the solid prolongations or downgrowths from the epidermis, which spread out in different directions or on section give rise to masses of alveoli of various shapes and sizes lying in a connective tissue stroma. In the characteristic members of this group the epidermal characters are preserved and result in epithelial pearls.

In tissue undergoing malignancy certain changes take place which indicate the vegetative activity of the cells. These are a smaller cell with oval or rounded cell body clear cytoplasm and a relatively large, deeply staining nucleus; the relations of the cells to one another become changed, they become crowded and occupy a much smaller space than under normal conditions. This is

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especially true of the basal-celled tumor and it is not so difficult to make a diagnosis in these cases of early epithelioma. In the squamous-celled type, however, particularly those which develop on ulcerated surfaces, it is not so simple to say whether one is dealing with tumor formation or only atypical proliferation. In chronic ulcerations there is a marked tendency for the epithelium at the edges of the ulcer to grow irregularly downward and infiltrate the tissue beneath. These processes may become snared off and sometimes develop pearls, when it is practically impossible to determine from the histology the exact pathologic condition.

Figure 13 shows the type of squamous-celled cancer of the skin. This growth had a rapid clinical course as the result of an injury to the leg nine months previously, and was followed by a secondary development in the neighborhood, due probably to transplantation of cells from the original focus. The alveoli which go to make up the tumor have one or more centers of pearl formation; their periphery corresponds to the basal layer, consisting of small cells with deep-staining nuclei. Within this are several rows of prickle-cells with a concentric arrangement; the majority have lost their prickles and are in various stages of keratinization, appearing as more or less flattened or rounded plates, anuclear, or with nuclei undergoing disintegration. As a rule the activity of pearl formation is an indication of malignancy. In the corium or supporting stroma is usually found an inflammatory reaction of varying grade. Not infrequently a mucinous degeneration has taken place, or the tissue is porous, or shows other signs of loss of vitality.

Of the basal-celled epitheliomas the rodent ulcer may be taken as the type, as it is the form most frequently met with. These tumors are made up of an undifferentiated type of cell, yet, contrary to the rule, are the least malignant of epithelial tumors. Various degrees of anaplasia are met with and a more or less spherical, polygonal or even spindle-shaped cell may be encountered. Not only the cellular morphology but the general structure of these basal-celled tumors varies and has led to the recognition of certain well-defined types. It has been suggested by Darier that this varied architecture might be explained as the attempt on the part of the

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basal layer to functionate, as during embryonic life, in the production of the appendages of the skin.

Descriptions and illustrations of cylindroma and tricho-epithelioma will be found in a paper previously published,[5] and of benign cystic epithelioma and other forms of growths in papers likewise already published.[7]

The picture of the ordinary rodent ulcer differs a great deal in appearance and may, in one instance, appear as a solid downgrowth from the surface epithelium, with little tendency to branch; in another the larger masses may show central cystic degeneration and peripheral budding, or fine or coarser processes of cells bifurcate throughout the cutis. Figure 14 illustrates a rodent ulcer near the ala of the nose originating from the hair follicles and forming solid tubes or cords of cells which give off lateral processes. Tricho-epithelioma, which also develops from lanugo hair follicles, has a somewhat different structure, which may be due to an attempt on the part of the cells to differentiate. These growths clinically may appear as morphea-like lesions, as already described.[5]

A frequent concomitant of the basal-celled tumor is the hyalin or mucinous degeneration, which affects either the cells or the connective tissue, or both. Degeneration is considered by some authorities, as Adami, to indicate malignancy, but in the skin we find the tumors most prone to degenerate are of a benign type. In mucinous or pseudo-mucinous degeneration the cells appear as in Figure 15, indistinct and poorly differentiated, in areas breaking down and forming cystic cavities which contain the products of degeneration. Aside from these changes there may occur a central autolysis of cells (Adami) which may be due to lack of nutrition or to metabolic products of the tumor cells themselves. Extractives or

7. Clinical and Pathological Observations on Some Early Forms of Epithelioma of the Skin, New York Med. Jour., June 9 and 23, 1900; and Cancer of the Skin, Jour. Cutan. and G. U. Dis., 1902, xx.

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diffusible products *in vivo* may have the same effect in producing this autolysis as the introduction of a vaccine from a tumor.

MULTIPLE EPITHELIOMATA

Many multiple epitheliomata in the early stages closely resemble Paget's disease. They present all grades from pale and red scaling patches, the size of a split pea or smaller, to patches as large as the hand. They have sharply defined, scalloped margins showing very slight tendency to elevate or pearly rolled edge. Some of them maintain their red and scaling appearance and others become the sites of fungating growths (Fig. 16). These tumors often develop on patches of seborrheic dermatitis, which suggests some infectious agent. It is possible that the bottle bacillus, in combination with the staphylococcus, stimulates epithelial proliferation. Even in the early stages, before any apparent thickening of the epidermis is present, proliferation of the basal layer can be determined by histologic examination.

CONCLUSIONS

A study of skin cancers suggests to the observer, if it does not demonstrate absolutely, that no one agent is concerned in the malignant proliferation of epithelial tumors and that cutaneous carcinomata have a multiple etiology. The development of epitheliomata following exposure to sunlight, *x*-rays or other radiant energy is a strong argument against the parasitic nature of the disease. Likewise, the occurrence of epitheliomata in xeroderma pigmentosum and allied conditions of the skin which come on in old age or middle life is an additional argument against this theory. These conditions are preceded by changes identical with those met with in xeroderma pigmentosum, such as a dry atrophic skin, telangiectases, warty growths and, finally, malignant transformation. Furthermore, the action of chemical substances on epithelium, for which they have a special

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predilection, such as arsenic, tar, scarlet R., tobacco, etc., demonstrate that a variety of agents have the power to stimulate epithelial mitoses which may pass into malignancy. Cancers which develop on scar tissue or antecedent conditions of the skin like lupus, syphilis, etc., suggest that we are dealing with misplaced cells in some cases and in others with degenerative processes which lead to the abolition of the functional activity of the cells, which is followed, as a consequence, by vegetative activity, according to the theory of Oertel, Adami and others. In primary multiple epitheliomata we have several foci in which an infectious agent or some internal sensitizing agent may have acted on the cells and rendered them susceptible to a local factor.

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PATHOLOGY OF MALIGNANT DISEASES OF NON-EPITHELIAL FORMATION *

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There are some fourteen different types of simple tumors. Each is due to the proliferation of one variety of cell. The epithelial tumors form the largest group of the simple tumors and their pathology has already been presented to you. The remaining tumors are often called the connective tissue tumors because many of them are of mesenchymal origin. The broader and better term to designate them when placed in contrast with the epithelial tumors is the non-epithelial tumors. It remains for me to present to you as dermatologists certain points of interest concerning the pathology of this large variety of tumors, some of which you see frequently, others rarely or not at all.

CLASSIFICATION AND TYPE OF CELL

A word first in regard to the classification of tumors. Under every recognized variety of tumor should be grouped both the slowly and the rapidly growing tumors built up by the multiplication of the same type-cell. In no other way is it possible fully to understand each variety of tumor and find out its characteristics. The type-cell is the one important element in every tumor. From it the tumor should be named; not from some peculiarity of minor importance, such as method of growth, arrangement of cells, or form of retrograde change. I shall speak briefly of some of the type-cells

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and of the tumors built up from them, and shall illustrate my remarks with numerous lantern slides.

The fibroblast, the ordinary connective tissue cell, is in general a flat cell with a flat, oval nucleus. It is characterized by the production of two kinds of fibrils, fibroglia and collagen fibrils, which may be stained differentially and which distinguish it from all other cells. The fibroglia fibrils are in intimate contact with the cytoplasm; the collagen fibrils form a true intercellular substance.

The slowly growing tumors arising from fibroblasts are called fibromata: the rapidly growing ones, fibrosarcomata. These terms represent extremes in rate of growth: all gradations between them exist. No matter how rapidly these tumors grow the cells tend to differentiate as do the normal fibroblasts.

The tumors known as keloids are formed by the proliferation of fibroblasts, but the cells tend to arrange themselves in thin sheets between broad layers of collagen fibrils, so that a striking and characteristic microscopic picture results.

The so-called myxoma and myxosarcoma develop from fibroblasts. They do not differ from the fibroma and fibrosarcoma except in the presence of fluid containing a variable amount of mucin between the collagen fibrils. The same holds true of the cells in the umbilical cord. These tumors do not deserve, therefore, to be regarded as a special type of tumor but should be looked on as a variety of the fibroma and fibrosarcoma.

The so-called giant-cell sarcoma, usually occurring in connection with bone, deserves special mention. At least two types of giant cells occur in tumors. One type is due to multiple mitoses, and occurs in a variety of tumors, for example, glioma, fibrosarcoma, lymphocytoma. It is a true tumor-cell with the characteristics of the other tumor-cells and signifies usually rapid proliferation under very favorable nutritive conditions. Tumors containing these giant cells are rarely or never

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called giant-cell sarcomata. That term is reserved for tumors containing giant cells of another type which are not due to multiple mitoses but to fusion of endothelial leucocytes to form foreign-body giant-cells. The leucocytes are attracted into the tumor usually by bone injured in some way by the growth of the tumor. They form foreign-body giant cells (osteoclasts), just as they do around bone requiring removal under normal and pathologic conditions. Their occurrence in tumors signifies usually erosion of bone, rarely the presence of free fat and fat crystals or other substances. They occur most commonly therefore in fibromata and fibrosarcomata involving bone. They occur also in inflammatory processes. Epulis, the term commonly applied to giant-cell formations about the jaws, is probably often only an inflammatory new-formation, not a true tumor. The presence of the giant-cells leads to a wrong diagnosis. This view is favored by the simple treatment needed to get rid of most of these lesions. Giant-cells of this type are therefore not true tumor-cells, and hence should not be mentioned in naming the tumor. That must be diagnosed and named from a study of the rest of the tissue minus the giant-cells.

The smooth muscle cell is a long spindle-cell with a rod-shaped nucleus. It is characterized by having longitudinal striations or fibrils in the cuticle. These fibrils fuse together at each spindle end of the cytoplasm to form a fairly coarse fibril of considerable length. From the smooth muscle cell arise slow and rapidly growing tumors called leiomyomata. These tumors occur occasionally in the skin, both single and multiple. The rapidly growing tumors are rare.

The fat-cell is characterized by the storage of fat within its cytoplasm. It is a cell of mesenchymal origin which produces no intercellular substance and which in the embryo and in young emaciated children resembles to some extent a liver-cell, with finely granular cytoplasm. (Fig. 1). In this early stage the fat when pre-

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sent is usually in small droplets and the nucleus remains centrally located. In the adult type of cell the fat is in one large drop and the nucleus is pushed to the periphery.

The ordinary tumor, the lipoma, resulting from uncontrolled growth of fat-cells, is composed of fat-cells of the adult type and is too well known to require description. Rarely, however, a rapidly growing lipoma may arise in which the cells (Figs. 2 and 3) are all, or for the most part, of the embryonic type with granular

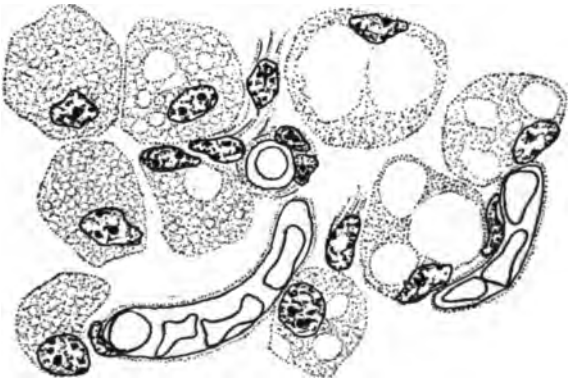

Fig. 1.—Fat cells of embryonic type.

cytoplasm in many of the cells and the fat in small droplets surrounding the nucleus, which is situated in the center.

Neuroglia-cells are characterized by the production of but one kind of fibril, the neuroglia fibril, which is in intimate contact with the cell producing it. Gliomata, the tumors arising from neuroglia cells, occur ordinarily only within the central nervous system, but they may arise rarely in the nasal sinuses and over the coccyx beneath the epidermis; in the latter region from remains of the neural canal. Two cases arising in this situation and carefully studied were distinctly infiltrative in their manner of growth and in one case metastases took place into both groins.

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The pigment-cell (chromatophore) occurs in the skin, the eye, and the membranes of the central nervous system. In the skin the cell is of mesenchymal origin. It varies much in shape, that is, it is polymorphous, produces no intercellular substance, and is characterized by the property of producing a brownish pigment. Abnormal collections of pigment-cells in various stages of development, with and without pigment, frequently occur in the skin. They are known as congenital nevi.

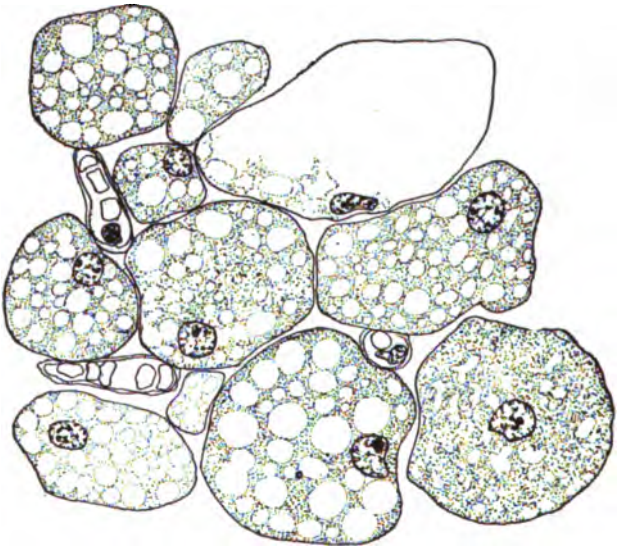

Fig. 2.

The tumors arising from pigment-cells are generally called melanomata. The cells composing them vary much in shape, from spindle to round, and also in size. The pigment varies greatly in amount. Many cells and clumps of them contain no pigment; others have so much that it is difficult to find the nuclei. The arrangement of the cells varies also; some tumors, composed of bundles of spindle-cells running in different directions, suggest a fibrosarcoma, especially if pigment is slight or absent. In other tumors the cells may show more or less

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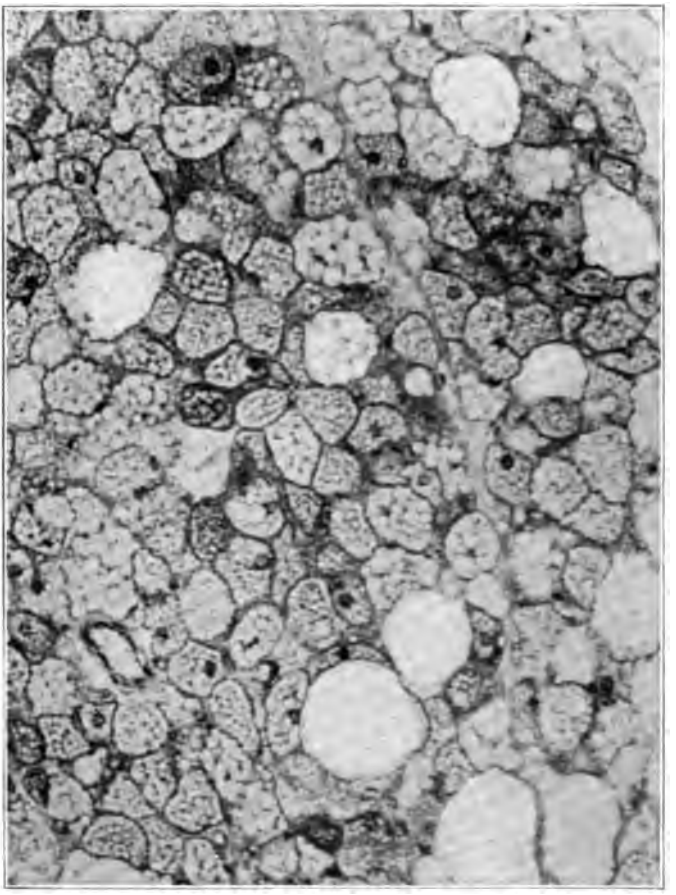

Fig. 3.

Figs. 2 and 3.—Lipoma composed of fat cells of embryonic type.

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of an alveolar arrangement, but usually little stroma is developed. Frequently by necrosis, dissolution, and absorption of cells at a distance from the blood-vessels, sheaths of tumor-cells are left around the blood vessels suggesting a perithelial type of growth.

The endothelial cell is poorly characterized except by the lack of distinguishing features other than that of lining vessels and spaces. Three varities are recognized, those lining blood and lymph vessels, which are nearly related and perhaps identical, and those lining the subdural space. I shall speak here only of blood-vessel endothelium.

The tumors arising from endothelial cells should be called endotheliomata. Most pathologists at present, however, reserve this term for the rapidly growing tumors and speak of the slow growing ones as angiomata. To distinguish this group of endotheliomata from the two other types the term hemangioendothelioma is advisable. Two varieties are recognized, the capillary and the cavernous hemangioendotheliomata.

The capillary form always grows infiltratively, not expansively. It invades fat and muscle-tissue, nerves, and blood vessels. In spite of its growing in an infiltrative manner, I know of but one case on record in which metastases took place. These tumors are prone to recur, however, after removal because the surgeon does not remove a sufficiently wide margin of apparently normal skin.

These tumors may grow slowly or rapidly and may be very destructive locally. Certain peculiarities of structure deserve mention. The endothelial cells may thicken up so as to form several layers around the lumen and mitoses may occur in any of these layers. If the lumen becomes obstructed in any way from hemorrhage or pressure the endothelial cells continue to multiply, forming whirls; less often they form irregular masses suggesting the alveolar arrangement of a carcinoma; lumina are not reformed. The connective tis-

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sue cells around the blood vessels of the stroma, in part grow in between the endothelial cells, in part deposit collagen fibrils between them so that the tumor may come to resemble fairly closely a fibrosarcoma; but the whirls of cells and the lack of fibroglia fibrils betray it. Moreover, the tumor in typical form may be found invading the fat tissue outside the tumor nodules.

Rarely all the vessels are surrounded by several layers of endothelial cells so that a perithelial type of tumor is suggested. Still more rarely papillary masses of endothelial cells may project into the lumina of vessels. Direct growth of this tumor itself within blood-vessels is not so rare.

The cavernous type of the hemangioendothelioma is not very common. It consists of large blood-spaces separated by thin partitions of connective tissue lined on each side with endothelial cells. These tumors may spread and give rise to different nodules, which follow in a chronologic sequence and yet seem to have no direct relation to each other. The explanation of the sequence of events is simple. The tumor grows within blood-vessels, extending along them and dilating them. In places it destroys or ruptures them and forms the large nodules so evident macroscopically.

There are many varieties of nerve-cells in the central nervous system. The one common and distinguishing characteristic of them all is the production of nerve-fibrils.

Tumors arising from nerve-cells are called neurocytomata.[1] They are probably not so rare as commonly supposed. They arise most frequently in the adrenal glands and may give rise to multiple metastases within the skin, bone marrow, liver and lymph nodes. The tumors in general suggest a lymphocytoma of the large cell type but they have one distinguishing feature—bundles of delicate fibrils running parallel. The nuclei

1. For the lantern slides of the neurocytomata shown I am indebted to Dr. J. H. Wright.

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of the cells are relatively large and the cytoplasm is small in amount and poorly defined. Occasionally, apparently when the fibrils are poorly developed and short, small clumps of fibrils are found with the cells arranged more or less in a circle around them to form a sort of rosette.

CONCLUSIONS

In conclusion I wish to say that it is advisable so far as possible to discard certain loose and indefinite terms frequently used in connection with tumors and strive for definite diagnoses and exact terms. For example, spindle-cell sarcoma refers only to a tumor with cells of a certain shape. The commonest tumor which grows rapidly with cells of this shape is the fibrosarcoma, but other tumors which may have cells of this shape are the chondrosarcoma, the osteosarcoma, the hemangioendothelioma, the leiomyoma, the rhabdomyoma, the glioma.

A round-cell sarcoma is most often a lymphocytoma, but other tumors which may have round cells are the osteosarcoma, the leiomyoma, the glioma, the myeloma, and the neurocytoma.

The so-called perithelial angiosarcoma is in my experience most commonly a melanoma, but other tumors which may grow in this form as the result of malnutrition (necrosis, dissolution, and disappearance of cells at a distance from the blood vessels) are fibrosarcoma, glioma, neuroma, and carcinoma (of breast and epidermis).

True tumor giant-cells occur in many tumors, glioma, fibrosarcoma, lymphocytoma. In the so-called giant cell sarcomata, the giant-cells are foreign-body giant-cells due to the fusion of endothelial leucocytes. They are not tumor-cells and should not be named in the diagnosis. The tumor itself is usually a fibroma or a fibrosarcoma. It may be only inflammatory tissue full of giant-cells. Probably the so-called epulis of the jaw is frequently of this nature, and not a tumor.

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THE SURGICAL TREATMENT OF CUTANEOUS MALIGNANT GROWTHS

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Before any surgical treatment for a cutaneous growth is planned or carried out there must be an accurate diagnosis. I cannot go into the details of such diagnosis for the different lesions, but I wish to emphasize in the beginning of this discussion the importance of a definite diagnosis. In some instances the diagnosis can be made from the clinical appearance of the visible cutaneous lesion. Palpation of the dermal or epidermal tumor should always be combined with careful inspection, and in many cases the recognition of carcinoma is possible by palpation when inspection leaves a doubt in the surgeon's mind.

When the diagnosis is impossible or doubtful from the clinical history, combined with inspection and palpation, a surgeon who has the requisite special training can differentiate the various pathologic processes by making an incision and thus exposing to the naked eye the freshly cut lesion. The operation follows immediately. Such an exploratory incision should be disinfected either with pure phenol or the Paquelin cautery. When the surgeon has not this special training, a small piece can be excised at the exploratory incision for a frozen section, and the diagnosis can be made almost immediately by the pathologist connected with the surgical clinic. It is unfortunate when a piece is excised for diagnosis and some days elapse before the

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operation is instituted. In the benign, and perhaps in some of the less malignant, skin lesions there is no danger from such a course, but, as far as my investigations have gone, it is distinctly contraindicated in the more malignant lesions, both carcinoma and sarcoma. If circumstances are such that the surgeon is compelled to excise a piece for diagnosis and then wait a few days before carrying out the operation indicated by the pathologic report, he should attempt to cut out the area from the tumor proper, without carrying his incision into the border of uninvolved tissue, and, in addition, the raw surfaces should be immediately treated with pure phenól or the Paquelin cautery. It is my opinion, however, based on a large experience and confirmed by the expressions in the literature, that the diagnosis can and should be made immediately. It is the hope that it may be possible to train ourselves to such a degree that even the exploratory incision for gross inspection or frozen section may become less and less frequent.

This positive diagnosis is necessary, because for the different skin lesions the magnitude of the operation varies, even involving considerable mutilation. It is especially in those cases where the extensive operation would be mutilating that the positive and immediate diagnosis becomes more and more essential. When the more extensive operation would be no more mutilating than the restricted local operation, I should advise the extensive operation if there be any doubt.

The extent of the local operation, and whether it should be combined with the removal of neighboring lymphatics, or deeper tissues, muscle and bone, varies not only with the nature of the lesion, but with its site. In general, it may be stated that for sarcoma a local operation is sufficient, while in carcinoma of the squamous or spinal-cell type, the local operation should, in the majority of cases, be combined with the dissection of the neighboring lymphatic glands and surrounding

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tissues. But to-day, no such general statements are sufficient. Experience has taught us that the nature of the operation must vary not only with the different varieties of tumors, but with the same tumor in different localities and different tissues.

So much to emphasize the importance of a positive diagnosis.

CLASSIFICATION

In the Surgical Pathological Laboratory of the Johns Hopkins Hospital I have developed a scheme of classification which has been found of practical value for teaching purposes and for investigating the question of the proper operation for the different tumors in the same locality.

In this investigation I have borne in mind the question, what operation will give the patient the best assurance of a cure with the least mutilation, and when and where is extensive mutilation justifiable in an atempt to acomplish a permanent cure?

The facts of this paper are based on a study of the following cases which include only lesions of the skin:

Malignant pigmented moles	**65 cases**
Sarcoma of the derma	**45 cases**
Epithelial tumors of the skin and mucous membrane	**812 cases**

These figures demonstrate that the most common malignant lesion of the skin is of epidermal origin; sarcoma is relatively rare.

MALIGNANT PIGMENTED MOLES

The study of this malignant dermal tumor of congenital origin, and of its benign prototype, brings out better than the study of any other group of neoplasms a conception of what may be called the preventive measures for treatment for malignant tumors. I look on a preventive measure as the recognition of those benign

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tumors and conditions which have a tendency to later become malignant, and their removal in the benign state.

I was the first, or at least one of the first, to call attention to the importance of the removal of certain forms of benign congenital pigmented moles, some seven years ago.[1] The statements then made, which were based on a relatively small experience, have been confirmed by the greater experience of the seven succeeding years. I now have careful personal notes of 65 cases of malignant pigmented moles. These cases have been collected from various sources. In every instance the diagnosis has been confirmed by a pathologic examination. Up to the present time there is not a definitely cured case amongst them. Now, it is to be remembered that in every one of these cases there had been a tumor visible to its host for many years. Such tumors can be removed under cocaine or local anesthesia without difficulty. It seems, therefore, worth while, to educate the public, to call the attention of the physician to such apparently innocent tumors, and to educate the physician to recognize when their removal should be urged. Of course, no harm can be done by the removal of any such tumor, although it may be practically impossible to remove all the pigmented areas which are to be found on some individuals.

In my experience with 65 malignant cases, in only three or four were the patients covered with such pigmented areas. In the majority, the individual had but one, or at most but a few, congenital pigmented moles. The mole which had become malignant was never a flat pigmented area, not elevated above the epidermis, but was distinctly a projecting tumor. It is my opinion that all such moles should be removed, especially when they are in localities exposed to trauma. Pigmented spots are entirely different from the definite, projecting, sessile or pedunculated, warty or smooth, pigmented mole.

1. Prog. Med., December, 1903, p. 149.

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This information should be given publicity. During the same period in which I have collected 65 cases of malignant pigmented moles, I have accumulated in the laboratory 76 benign, the majority of which have been removed by myself, because of my attitude toward such apparently innocent tumors. As to the present result in all these cases, I have a record with but few exceptions, and there have been no local recurrences and no deaths from internal metastases. The largest number of moles removed from any one individual was five. In every case the mole has been removed with the knife, and not an individual finds any fault with the scar.

I emphasize this point, because there are other methods employed to remove different types of benign skin lesions—the *x*-rays, radium, carbon-dioxid snow, liquid air, the Paquelin cautery, the electric needle, and different caustic pastes. As I have had no experience with these methods of treatment, I am not justified in condemning them, but I am inclined to the view that the more dermatologists familiarize themselves with the simplicity of removing small skin tumors with the knife, under local anesthesia or nitrous oxid gas, the more they will employ this method.

For certain tumors and in certain situations the above methods have a distinct place, but for the benign mole I would urge complete excision with the knife. With the other methods there is not the same certainty that all these congenital residues of cells are destroyed, and when the method is employed incompletely it may act as a stimulant. In a number of my personally studied 65 cases of malignant congenital pigmented moles, one of these methods had been first employed. Of course, it is impossible to say that this tinkering with the mole was the factor which produced its malignant growth. Nevertheless the observation is suggestive.

The excision with the knife may be just as dangerous if the tumor is not given a sufficient berth. I am confident that it is better to leave a mole alone than to ex-

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cise it incompletely. When the mole is situated on the face there is a temptation in the hands of an inexperienced surgeon to limit the area excised, but as a matter of fact the scar is no more conspicuous when sufficient margin is given than otherwise.

The public and physicians should be impressed with the importance of the immediate and complete removal of any congenital mole which suddenly shows any growth, superficial ulceration, or scab formation. The sudden appearance in the skin of a tumor resembling a congenital pigmented mole should be looked on as an indication for its immediate removal.

I trust that the subject of the relation of benign or innocent tumors to later malignant transformation will be more often considered in the dermatologic and other sections of the American Medical Association. There is great need for publicity. It is true that the relative number of individuals to be saved is small, but certainly large enough to justify the time and trouble.

The first problem in regard to our attitude towards the apparently benign or innocent mole, I think should be looked on as settled—the tumor should be removed.

The second problem is by no means settled; that is, what should be the extent of the local operation, and should the neighboring lymphatics be included in the dissection when the patients present themselves with a mole which shows, clinically, definite signs of malignant growth?

In my 65 cases and, as far as I can ascertain, in the literature, surgeons have confined themselves to the local operation when the neighboring lymphatics were not visibly involved. Many of the patients, before there is any evidence of general metastasis, return with enlargement of the neighboring lymphatics, and now the more complete operation is performed. In many cases, if glandular enlargement is evident, the complete local and glandular operation has been carried out in the first instance. But there have been no permanent cures. In

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view of this evidence it seems to me I am justified in urging that in the future surgeons perform in every instance, whether there be visible glandular enlargement or not, a larger local operation combined with the complete dissection *en bloc* of the neighboring lymphatics, and such an operation should be planned along lines similar to Halsted's complete dissection for carcinoma of the breast. That is, the tumor should be removed with a zone of uninvolved skin and a wider area of subcutaneous fat, and with this should be included at least the fascia, and, in some cases, the muscle itself, then the neighboring lymphatic glands and surounding tissue. It is my opinion that we are distinctly justified in the future in attempting such an extensive dissection, although at the present time we have no evidence that the results will be any better.

But, as I study critically the 65 cases of which I have records and the available literature, I am impressed with the conclusion that the surgery of moles in their malignant state has been incomplete. There is therefore room for improvement in two directions: The education of the public and the profession in such a way that we may get the mole either in its benign state or very quickly after the first signs of local growth, and, second, in the later malignant state we must give the tumor a wider berth and combine the dissection with the removal of the neighboring fascia and lymphatic glands.

Duration of Life.—The duration of life in the malignant pigmented mole varies, so that in some cases the surgeon will feel that he has accomplised a cure. Estimating the duration of life from the onset of the first signs of local growth to the date of death, irrespective of the intervening operation, I find the following facts: Five patients died within one year, one of these within six months; 8 lived from one to two years; 6 from two to three years; 4, three to four years; 2, four to five

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years; one of my patients lived six years and eight months; the remainder of the patients are recent cases or still living at periods of from two to five years. It is unusual, therefore, to have a duration of life of over four years. Among the patients living and apparently well to-day the longest in point of time is that of Dr. Wainwright of Scranton, Pa., who sent the tissue from his case for examination. In this case at the first operation the malignant mole and the glands in the axilla were removed; one year later the glands in the opposite axilla were removed; the primary tumor had been present four months before the first operation, and it is now five years since the beginning of its growth; the patient is well and there is no evidence of metastasis. This case was reported by Dr. Wainwright in 1905.[2]

Even if we do not acomplish an ultimate cure we may demonstrate that we at least add to the comfort of the patient during the time he has to live. One can feel quite positive that Wainwright's patient, even if she ultimately succumbs to internal metastases, has been more comfortable, and I have other similar cases of patients who have, however, not lived as long.

I repeat, therefore, that surgeons should, for the malignant mole, perform in the first instance a more extensive operation. Local growth in a congenital pigmented mole, even with slight ulceration, is not always associated with malignancy, but the differential diagnosis is so difficult that I should advise in every instance that such local changes be considered malignant.

Age of Onset.—Among my 65 cases the age of the onset of the malignant change in the mole has been between 30 and 76 in all but 11 cases; the youngest patient was 10 years of age. We should, therefore, look for and urge the removal of such moles when opportunity offers in patients under 30.

2. Tr. Lackawanna Co. Med. Soc., 1905, I, 141.

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SARCOMA OF THE DERMA

In this group, in which there are 45 cases, there is generally a history of a congenital nevus, an acquired or congenital fibroma, or the tumor has originated in scar tissue. The type of the tumor, when there has been a history of a nevus, is one that would naturally be expected—angiosarcoma. With a few exceptions the malignant connective-tissue tumor which has its origin in a scar or fibroma is of the type of the fibro-spindle-cell tumor. Among 14 cases of the former type (angiosarcoma) I have observed but one cure, and it is important to note that in this case a more extensive local and glandular operation was performed than in any other. Among 26 tumors of the latter type (fibro-spindle-cell sarcoma) 20 patients have been permanently cured by a local operation only.

Angiosarcoma.—Among 14 cases in which the gross and cellular pathology of the tumor has been practically identical, in 6 cases the malignant neoplasm has arisen in a congenital vascular nevus; in 8 there was no such history.

During the same period I have observed 109 cases of benign hemangiomas. The tendency, therefore, for the congenital nevus to become malignant is distinctly less than in the congenital pigmented mole.

All of the 109 cases of benign hemangioma have not been confined to the skin; for example, there are 7 situated within muscle—the so-called intermuscular angioma. Here the differential diagnosis is not a problem of dermatology.

There are 9 cases of the so-called fibroid or elephantoid hemangioma; 5 of these are of dermal origin; they are as follows:

Pathol. 5,151; pedunculated tumor of the ankle; male, aged 42; tumor twenty-three years.

Pathol. 7,249; pedunculated tumor of skin of back; female, aged 16; tumor five years.

Pathol. 7,919; small pedunculated tumor on skin of back; male, aged 21; tumor congenital.

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Pathol. 4,698; pedunculated tumor of skin; no other history.
Pathol. 9,999; sessile tumor of skin of neck; aged 26; tumor congenital.

It is to be noted that in all these cases the tumor had been present many years; all of them were of the type which indicated removal at the onset. In these cases, however, the local growth, although very cellular in places, still remained benign, and the patients have remained well since the local excision. In a few associated with the local growth there has been superficial ulceration of the epidermal covering, but no fungus formation, which is generally the case in sarcoma when ulceration takes place. In some of these cases, clinically, the diagnosis of sarcoma had been made. One not familiar with this type of tumor might conclude from the histologic study that they were sarcomas. In the gross the section showed red, spongy areas from which blood can be expressed, and the cellular, white fibrous areas; that is, the tumors have a mottled red-and-white appearance; pigmentation due to hemorrhage is generally seen. Microscopically the picture is a varied one: the vessels of the angioma are present in the red areas; quite frequently the endothelial cells show proliferation giving the appearance of an endothelioma; in the white areas the vessels are absent or plugged with endothelial cells, and this white tissue is composed of quite cellular connective tissue, in which there are numerous areas of blood pigment easily differentiated from the pigment of the congenital mole, benign or malignant. If these tumors were included among the sarcomas of the skin the number of cures would be increased, but I am quite certain that they are benign, because the remaining four cases were situated either about tendon-sheaths or within muscle, and the tumor tissue was not completely removed, because such complete removal would have led to amputation or mutilation. Nevertheless, these patients have remained well, in two of the cases six and ten years since the operation. When the tumor is situated in the skin

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the problem is a simple one, because complete local operation is possible without mutilation. The tumor may be called what you like, but the patients remain well. When situated deeper the differential diagnosis, in some instances, becomes essential to avoid unnecessary mutilation.

Granulation-tissue Tumors.—Here the differential diagnosis is more difficult. I have records of six cases. The age of the patients varied from 9 to 25 years, the duration of the tumor from two weeks to three months. In every instance there was the history of an injury, and the little tumor composed of red, vascular granulation tissue has grown from the scar. On account of the situation of these tumors a correct diagnosis is important, because if they be looked on as sarcoma a complete local operation, in some instances, would result in unnecessary mutilation. In two instances the tumor was situated at the site of the toe-nail; in one of these cases an unnecessary amputation was done. In three instances the tumor occupied the palm of the hand, once the finger and once the skin of the axilla. In these cases, if the surgeon is not able to make a differential diagnosis clinically, a trained pathologist should do so from the frozen section. When complete excision would cause mutilation these areas should be treated with the Paquelin cautery. The difficulties of differentiating sarcoma from granulation tissue is an old problem in the history of pathology, but it can be done and often saves the patient disfigurement.

Hemangioma of Skin.—Among my 87 cases of hemangioma the majority have been dermal tumors, and most of these of congenital origin, although in many cases the tumor was first observed later in life. My figures by no means give an idea of the relative frequency of this tumor, but represent only the type which, on account of local growth, has caused its host to seek surgical aid. During the last twelve years there have been sent to me for examination, from various sources, ten cases with the

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diagnosis of sarcoma. In all of these cases the dermal tumor in its growth had caused the destruction of the epidermal covering and given rise to a very vascular granulation-tissue mass. When I compare these cases clinically with true sarcoma I find a distinct difference: in sarcoma the compressibility of the tumor beneath and around the granulation area is lost, while in the benign tumor the characteristic feature of angioma—compressibility—is present. The differential diagnosis from a frozen section should not be difficult: in the angioma the blood-containing vesels are always present and the cellular tissue between these vessels resembles ordinary cellular granulation tissue, while in sarcoma no such picture is observed. The differential diagnosis is important, because the complete excision of the benign lesion would frequently be mutilating, and a cure can be accomplished by partial excision in conjunction with the Paquelin cautery, liquid air or carbon-dioxid snow. In view of the comparative rarity of sarcoma and the frequency of the hemangioma simulating sarcoma one should look on these lesions as benign until they are proved, by microscopic examination, to be malignant.

Sarcoma of the Skin with a History of a Congenital Nevus.—I have six cases in one of which the patient was cured. They are as follows:

Surg. 1,453; white, male, aged 46; congenital nevus in groin 2 cm. in diameter; at 23 years of age there was distinct growth with ulceration; within seven months the tumor had infiltrated all the tissues of the groin and was inoperable. The patient died four and one-half months later. In this case, at the first appearance of growth and ulceration a positive diagnosis should have been made, and the probabilities are that an extensive dissection at this time would have accomplished a cure.

Pathol. 637; white, male, aged 43; multiple nevi and moles of congenital origin; a nevus situated in the skin over the ribs began to grow, and, after it had been present three years, it was incompletely removed; there was immediate local recurrence with fungus formation. Now in spite of a complete operation death took place from internal metastasis in eleven months.

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The lesson from this case is distinct. At the time of the growth in one of these nevi it should have been completely removed, because it was situated in an area where even an extensive local operation would not have resulted in mutilation. Even at the end of three years there might still have been some chance of a cure if better surgery had been employed.

Pathol. 3,136; this patient was a white male, aged 43, who had observed a congenital nevus over the lower sternum; at the age of 23 it was the size of a twenty-five-cent piece; at that time it began to grow, but the growth was slow, and there was no ulceration for eight years; then, two years ago, it was incompletely excised. Now, on admission, in addition to the local ulcerating growth, which is intensely pigmented from hemorrhage, there is distinct involvement of the glands in the right axilla. At such a late period one could not expect much even from the most complete operation, but it was attempted. The patient died two years later of internal metastasis.

If this patient had sought the advice of a physician when the nevus first showed its local growth, at the age of 33, and the lesion had been locally excised then, the result undoubtedly would have been a different one.

Pathol. 4,707. This is the youngest patient of this series. The child was 4 years of age; the small congenital angioma was situated on the inner lower lid; before it was subjected to operation it had been present four months and reached the size of a small hen's egg; in its early growth there was a period in which a complete operation combined with the Paquelin cautery might have accomplished a cure.

Pathol. 8,225. This patient represents the oldest, a woman, aged 74; a small nevus on the cheek at this late period in life began to grow; it was constantly irritated by picking; when subjected to operation it was an ulcerated tumor with infiltration; a complete operation would have caused great mutilation. The somewhat incomplete excision did not accomplish a cure.

In all of these cases the sarcoma was of the perithelial type. The cells were small and round, very much like those of lymphasarcoma. This tumor, wherever I have encountered it, has shown a very high grade of malignancy, and up to the present time I know of no permanent cures.

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Cured Case of Sarcoma of the Skin in a Congenital Nevus

Pathol. 9,063. This patient was referred to me by Dr. William M. Babb, of Keyser, West Virginia. The woman was 67 years of age, and had observed a congenital tumor in the skin over the inner aspect of the right thigh; slight local growth had been observed three years, and when the patient scratched the thin epidermal cover there was slight bleeding. Three weeks previously an exploratory incision was made into the tumor without cutting into the surrounding uninvolved tissue; on account of hemorrhage the wound was packed; the local lesion was about the size of a silver dollar.

On account of its position I decided to do a very large local dissection which would be no more mutilating than a restricted one. The tumor was removed with a zone of uninvolved skin; the incision was carried to Poupart's ligament and the skin flap dissected back, exposing the entire inner and median surface of the thigh; this large area of subcutaneous fat was removed with the fascias of all the muscles and everything in the groin up to Poupart's ligament, including the fascia sheaths of the great vessels. Microscopically, the tumor is a spindle and round-cell angiosarcoma. In the tissue from the groin I could find no tumor cells. This patient was well two years after the operation.

The two points which I wish to emphasize in regard to congenital tumors of the skin are well brought out in the study of this small group of cases. Any growth in a congenital dermal tumor should be considered as a symptom of an acute disease. A diagnosis should be made at once; if the histology shows that the growth is still of an innocent character a restricted local operation will be sufficient. As has been pointed out, the congenital angioma may show growth of a benign character, and the nature of the local operation will vary with the position of the tumor; if complete local operation would cause mutilation one is jusified in using the Paquelin cautery or carbon-dioxid snow for these cases. In other situations I should recommend excision. If the histology shows the picture of sarcoma the local operation should be very extensive, and I am quite confident, if this is done, the number of cures will be increased. When the patient is seen later in the malignant stage of

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the disease it seems to me it is justifiable to make an attempt at a most radical dissection *en bloc*. The chances of a cure, however, are relatively small for the cellular type of sarcoma.

Angiosarcoma of the Skin with No History of a Nevus.—These 8 cases differ from the previous group only in the absence of a history of a congenital tumor. The age of onset has varied from 4 to 54 years of age; the duration of the tumor from six weeks to twenty years. In five of the cases the duration of the tumor has been over one year. In none of these cases has a cure been accomplished. All of them have been of the most malignant form of sarcoma—small-round-cell, and most of them of the perithelial type. All of the tumors first apeared as subepidermal nodules; in a few ulceration with fungus formation was present at the time of the operation. Three were tumors of the scalp, clinically resembling the ordinary wen, which is an epithelial cyst; two of thes were blood-cysts; the third blood-cyst was situated between the mucous membrane and skin of the cheek. All of the important problems of the surgical treatment of tumors are represented in the study of this group. In the first place, the sudden appearance of an epidermal nodule, even if it has all the signs of a benign tumor, should be looked on as an acute disease. In view of the fact that in this earlier period a differentiation between the benign and malignant cannot be made, except at the exploratory incision, the surgeon should be prepared to make the differential diagnosis. Of the three tumors of the scalp resembling wens, in every one such a clinical diagnosis was made, and the incomplete excision sufficient for the wen was performed for the more malignant tumor. In all there was immediate local recurrence. Subepidermal blood-cysts are not always malignant; I have observed a benign blood-cyst in the cheek and one on the tongue. Both were recognized at the exploratory incision and a cure accomplished without mutilation.

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Sarcoma of the Skin in Scar Tissue.—I have personally studied 19 cases, in which 16 patients have remained well. In all of the cured patients the tumor was of the fibro-spindle-cell type. Tumors of this character must be looked on as on the border-line between benign and malignant. One pathologist may call them sarcoma, another a cellular fibroma. The important surgical fact is that these tumors are curable by a local operation, and such an operation need not be extensive.

When such a tumor is observed in a scar it is essential to differentiate, in the gross or in the frozen section, this fibro-spindle-cell tumor from the more malignant round- and spindle-cell sarcoma, and the latter must be differentiated from the carcinoma. I wish to emphasize this, because very frequently the operation which should be performed for the carcinoma, and in some instances for the spindle- and round-cell sarcoma, would be unnecessarily extensive and mutilating for the fibro-spindle-cell tumor. The differentiation can be often made by an experienced surgeon clinically; if this is not possible an exploratory incision or frozen section should settle the question at once.

The relation of scar tissue to various pathologic processes is an important one. The most common, non-ulcerating neoplasm is the keloid. I have studied 42 cases. It is important to differentiate the keloid from the fibro-spindle-cell sarcoma in scar tissue. There are cases in which there is little doubt as to the keloid on one hand and the sarcoma on the other. The keloid confines itself to the scar proper, reaches a certain size and ceases to grow; it rarely ulcerates. The sarcoma quickly infiltrates beyond the area of the scar, grows more deeply, and not infrequently ulcerates. The histologic differentiation from a frozen section in some cases is impossible, in my opinion. If there is any doubt in the diagnosis between a keloid and a sarcoma I should advise that the treatment be planned as for a sarcoma. Among the fibro-spindle-cell sarcomas in scar tissue I

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note a few cases in which cures have been accomplished after one or more recurrences, and the question naturally arises, Are these tumors sarcomas or keloids Perhaps later Dr. Mallory, who is making such important and interesting investigations into the cellular and intracellular structures of tumors, may throw light on the differential diagnosis. But at the present time there are many cases in the group of fibro-spindle-cell tumors in which the surgeon should not depend on the frozen section, but should be influenced more by the clinical picture and gross pathology, and when there is any doubt it is best for the patient to treat the lesion as sarcoma, because the necessary local operation is not of sufficient extent to cause mutilation.

I wish to emphasize here again that for this borderline fibro-spindle-cell tumor the local operation need not be very extensive. However, if the lesion is situated in a position in which a more extensive local operation will cause no greater mutilation I would advise its performance.

The granulation-tissue tumor I have already discussed under angioma and angiosarcoma. The more malignant spindle- and round-cell sarcoma in scar tissue is relatively rare. The three cases which I have studied died of local recurrence and internal metastasis. All of them were, in the modern sense, neglected cases, because the growth in the scar tissue had not been subjected to treatment until a period of from three months to two years had elapsed, and in all of the cases the first operation had been incomplete; two were later subjected to second operations of a more extensive character without avail. The investigation of the cured cases in this group shows in a few instances that the operation has been unnecessarily extensive. For example, in one in which the lesion was situated on the heel, amputation of the foot was performed.

The epithelial tumor which may form in the epidermis of scar tissue will be discussed later.

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The study of scar tissue is therefore a very interesting and important problem, both to the dermatologist and to the surgeon. A wound is an irritant and the injured tissues throw out or give rise to a new tissue which is at first very cellular, and is called granulation tissue, and later changes into scar tissue. If there is a defect in the skin or mucous membrane we have, in addition, an ulcer and the process of epidermization of such an ulcer. There is unusual activity, therefore, on the part of both connective tissue and epithelium.

During the early healing of a wound, if the inflammatory reaction is excessive, we have what is called a granulation-tissue tumor. In later periods an excessive scar tissue gives rise to keloids. If the wound is associated with a break in the skin we may have, during the epidermization of the ulcer, atypical down-growths of epithelium, or over-growths giving rise to a papillomatous surface at the ulcer edge. The malignant epithelial tumor—the carcinoma—is observed only after an ulcer has been present many years, but the sarcoma, apparently, may form at a much earlier period.

It is important, therefore, that every attempt be made to encourage the proper and prompt healing of a wound, and nothing should be done unnecessarily to increase the inflammatory activity of the cells.

This is not the place to discuss the relation of wounds and other lesions of the skin which keep up a form of chronic irritation, but if surgery of to-day is not to be the forlorn hope of an operation at the late stage of a disease, it must demand that it be given the opportunity, not only to apply its art in the early stage of neoplastic growth, but even at an earlier period, which might be called the percancerous period. At this period surgery advises the removal of all skin tumors and proper healing of all skin lesions.

Sarcoma and Fibroma of the Derma.—One is confronted with the same difficulty of differential diagnosis

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between fibroma and sarcoma as between the fibro-spindle-cell sarcoma of scar tissue and keloid.

I have classed 9 cases as sarcoma in tumors which have been present a number of years and which might be called originally benign fibroma. Four patients have remained perfectly cured since the complete local excision of the dermal growth. In every one of these cases the histology of the tumor exhibits the picture of fibro-spindle-cell new growth. In the three patients who were not cured the histology of the tumor was entirely different; they were round-cell sarcomas, and the round or spindle cells were found in alveoli, the mesh-work of which appeared to be the remains of the fibrous tissue of the old fibroma.

It is very important to call attention to the fact that in all of these cases there was a history of an apparently innocent dermal tumor which had been present from one to eighteen years. The actual duration of the tumors was as follows: One (2 cases), three, four, eight, ten and eighteen years. There was no difference in the local growth in these two types of tumor. In every case there was a quiescent period, then a local growth with superficial ulceration, in many cases associated with trauma. The cause of death in one of the cases was internal metastasis. In this instance the local growth of the tumor was insignificant; in the other two cases which succumbed to the disease there was, first, local recurrence after an incomplete operation, then again local recurrence and internal metastasis after an attempt at complete operation.

As compared with keloids the true fibroma of the skin is a less frequent lesion. I have recorded as true fibroma of the skin 28 cases; many were small nodules with adherent epidermis of from 5 mm. to 2 cm. in diameter, the majority about 8 mm. In many of these there was a history of a trauma, or the hard nodule was secondary to a pimple. That is, in almost every case there was an etiologic factor. So perhaps these tumors should be

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really classed as keloids. Among the 9 cases classed as sarcoma 3 in their onset were small subepidermal nodules, 4 pedunculated tumors.

It seems to me that this evidence is sufficient to jusify the immediate removal of the small subepidermal or pedunculated fibroma during its innocent stage. This should be done by a local operation. If the patient seeks advice after such a tumor has begun to grow the extent of the local excision should be relatively greater. I have already called attention to the fact that in two of the fatal cases of sarcoma the first operation at an apparently fairly early period was followed by local recurrence, due probably to a restricted local operation.

Fibromyxoma of the Derma.—Von Recklinghausen's disease is not very frequent, and the tendency of one or more of the dermal tumors to become malignant is unusual. I have one such a case. It is quite impossible in many of these cases to excise all of the tumors, but if the tumors are few in number, or if one begins to grow, I would urge the immediate removal by a local operation.

I have never observed a fibromyxoma or a pure myxoma occurring as a single tumor to be situated in the derma, nor have I observed a myxosarcoma of the skin.

Connective-tissue Cysts.—Among 30 cases of this type in only 2, one of the cheek and one of the tongue, were the cysts of dermal origin. Both were blood-cysts, and I have already discussed their differential diagnosis from sarcomatous cysts.

Lymphangioma of the Derma.—These are relatively infrequent lesions. All the cases which I have studied were benign. The diffuse form seen in the lip and tongue (macroglossia and macrocheilia) is not difficult to recognize. I have observed a small subepidermal tumor of the tongue of this type, and here the proper differential diagnosis from early epithelioma saved the patient from a mutilating operation. Another case is

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very rare: the tumor, 2 cm. in diameter situated in the skin of the thigh, had been present fifteen years in a male aged 47; it was encapsulated and showed a calcification and ossification. In a third case there was a diffuse growth in the groin which, on account of the accompanying papillary overgrowth of the epidermis, might have been mistaken for carcinoma. Gilchrist, who saw this patient first, has reported the lesion as lymphangioma circumscriptum.

Among the rarest benign tumors of the skin I have seen one case of xanthoma.

EPITHELIAL TUMORS OF THE SKIN AND MUCOUS MEMBRANE

Whether Krompecher's[3] classification be accepted or not, I am firmly convinced that a classification along the lines established by him is of practical importance.

There is a lesion of the skin which may appear as a wart, a subepidermal nodule, an ulcer or a fungus, and, microscopically, differs from the squamous-cell epithelioma. These tumors practically never give metastases and can be and are permanently cured by a somewhat restricted local operation. The opposite is true of the so-called squamous-cell epithelioma, in which the cells show hornification and pearly-body formation.

As with the benign and malignant connective-tissue tumors of the skin and the benign and malignant pigmented moles just discussed, so with the epithelial tumors, the extent and plan of the surgical operation should be controlled by the character of the tumor. As has been stated before in this paper, the same tumor when situated in different localities sometimes can be treated along different lines. For example, a squamous-cell epithelioma of the lip should always be removed locally, and this local operation should be combined with the complete dissection of the glands of the neck. But

3. Zieglers Beitr. z. path. Anat. u. z. allg. Path. (Zieglers), 1900, xxviii; Der Basalzellenkrebs, Gustav Fischer, Jena., 1903.

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for the same tumor situated on the scalp the glandular operation is apparently unnecessary.

In 1904 I contributed my experience[4] with epithelial tumors as based on 468 cases, and adopted, to a certain extent, the classification of Krompecher. With an increased experience—684 cases—I am still favorable to Krompecher's views.

In the breast, no matter what the variety of the carcinoma may be, there should be no restriction of the complete dissection, but experience has taught us that in the skin and mucous membrane the well-known different types of epithelial tumors, with their differences in local growth and tendency to local infiltration and metastasis, allow us to vary the operation according to the site and character of the tumor. This is important from the standpoint of the patient, because if the principles applied to the breast were found to be necessary for cancer of the skin, and mucous membrane many patients, in order to be cured, would be subjected to mutilation, which experience up to date has demonstrated to be unnecessary. It is fortunate for the patient with cancer of the breast that the most extensive operation is little if at all more mutilating than the restricted operation. In cancer of the breast there is the same variability in the character of the tumor, and, while for some tumors the probability of a cure is 80 per cent., in others only 20 per cent., experience has demonstrated that a restricted operation in the most favorable form of cancer of the breast will reduce its probability of a cure to that of the most malignant form of cancer subjected to the most complete operation. It is this evidence that prohibits any restriction of the operation for cancer of the breast.

In cancer of the skin and mucous membrane we are accumulating experience which forces us to change the plan of the operative technic. In some cases the operation must be considerably extended. For example, in

4. Progr. Med., December, 1904, p. 134.

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carcinoma spinocellulare (squamous-cell cancer) of the extremities, which rarely occurs except in wounds, ulcers or warts, it has been the rule in the majority of surgical clinics to confine the dissection to a local removal only. But to-day the majority of authors who have investigated the ultimate results emphatically conclude that the local operation should be combined with glandular dissection. In cancer of the tongue, it is my opinion that to-day the glandular operation is unnecessarily extensive, while the dissection of the floor of the mouth is too restricted.

TABLE 1.—EPITHELIAL TUMORS ACCORDING TO SITE AND PATHOLOGIC VARIETY

	Pathologic Variety						
Site.	Spino-Cellulare.	Cubo-Cellulare.	Baso-	Malignant Pigmented.	Benign Wart.	No Note.	Total
Lower lip	100	2	4	12	1	42	161
Upper lip	4	..	9	2	..	6	21
Face, cheek	9	3	24	5	5	28	74
Chin	..	..	2	..	..	2	4
Eyelid	1	1	16	..	..	13	31
Ear	6	1	4	1	2	3	17
Nose	12	..	24	5	4	9	54
Scalp, forehead	3	3	9	..	5	11	31
Mucous membrane of mouth, gum, hard palate	23	3	2	3	2	16	49
Tonsil, pharynx	3	2	1	..	..	7	13
Tongue	37	..	7	4	6	24	78
Skin of neck	1	..	5	1	1	2	10
Branchial cleft	3	9	4	..	..	7	23
Upper extremities	16	..	4	7	3	4	34
Lower extremities	13	3	1	2	10	6	35
Penis	13	..	4	1	7	12	37
Skin of body	2	..	5	1	3	1	12
Total	246	27	125	44	49	193	684

Table 1 illustrates the relative frequency of epithelioma of skin and mucous membrane in the different localizations. In the first column appear the figures of carcinoma spinocellulare (squamous-cell epithelioma). In the second column are recorded the cases of carcinoma cubocellulare, which is composed of transitional cells; this variety is relatively unimportant, as the malignancy of this tumor is practically identical with that of the spinal-cell tumor, and the treatment should be the same. In the third column appears the car-

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cinoma basocellulare; in the fourth, the malignant warts, irrespective of their cellular type, and in the fifth column, the benign warts. In the sixth column the number of inoperable cases, or those in which there was no pathologic examination, is noted.

For the basal-cell tumor and the benign wart a local operation is sufficient. There have been many reported cures of basal-cell ulcers and fungi after treatment with the *x*-ray, radium, caustics and carbon-dioxid snow. I have had no personal experience with these methods. I have operated on a number of cases in which these methods of treatment had failed in the hands of competent dermatologists and roentgenologists. I have never observed a recurrence after proper excision in operable cases. If the small rodent ulcer (basal-cell tumor) is situated in a position where the local excision would produce more or less mutilation, for example, the eyelid, the ala of the nose or the lobe of the ear, my experience teaches me that there is no danger in attempting a cure by the methods just enumerated, provdied the patient is carefuly watched. The chances of a permanent cure by local excision after a failure from any of these methods are not decreased. When the rodent ulcer has reached a huge size, practically prohibiting its removal with the knife, the other methods should be attempted, and now and then cures have been reported. I wish to emphasize the fact that experience demonstrates that an incomplete excision with the knife is more dangerous than a failure from the other methods, and if on account of the position of the epithelioma the surgeon feels that it would be less mutilating to give the lesion a somewhat narrow margin the knife should be supplemented by the cautery.

In my own experience, when these tumors have come to me in their early stage, I have no difficulty whatever in accomplishing a cure without mutilation, no matter what their situation, by excision with the knife, and I have followed the ultimate results in my cases most carefully.

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For the malignant wart a local operation is sufficient, but when the original wart has practically been destroyed and its position is occupied by an ulcer or fungus it must be treated according to the character of the cells of which it is composed. The great majority of warts are spinal-cell tumors. The basal-cell tumor rarely has its onset in a papillary wart; it appears as a subepidermal nodule, at first covered with brownish epidermis, and then, as it grows, with a scab; beneath the scab an ulcer forms which may remain an ulcer no matter how extensive, or may produce a fungus no matter how small the ulcer. We never observe fungus growth in an ulcer larger than a silver dollar.

STUDY OF EPITHELIOMA ACCORDING TO SITE

Epithelioma of the Lip.—Carcinoma of the lip is the most frequent of the malignant lesions of the skin and mucous membrane.

The public must be educated to the life-saving importance of immediately consulting the physician for any ulcer, induration, wart or scab at the mucocutaneous border of the lower lip. The surgeon, with the rarest exception, must never vary from the rule to remove the glands of the neck as well as the primary tumor of the lower lip. The experience in the study of 161 cases, of which I have notes, demonstrates the appalling neglect on the part of the patient and the profession of lesions of the mucocutaneous border of the lower lip. On the whole, surgery has been much less neglectful in restricting its operation. A lesion at the mucocutaneous border of the lower lip in the majority of instances is a carcinoma spinocellulare. I have observed but one benign wart, twelve malignant warts and four basal-cell carcinomas. In these 17 cases a local operation would have been sufficient; all have been cured.

Among 32 cases of carcinoma spinocellulare of the lower lip in which, for some reason, the tumor only was removed, I can find only two definite cures. In a few

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cases the patients were apparently well six years and then returned with carcinomatous glands in the neck. When these results are compared with those in which both the local and glandular operations were performed at the same sitting there is a tremendous difference. If we take the cases in which six years have elapsed we find at least 50 per cent. of the patients well, as compared with less than 10 per cent. when the glandular operation was not done. What the results will be when patients seek surgical aid earlier I am not prepared to say, but I think it would be a mistake, with the evidence in hand to-day, not to combine the glandular operation with the local, even when patients present themselves in the early weeks of the lesion. In one of my own cases, which has been cured, the epithelioma was so small that the section can be viewed in its entire extent under the low power of the miscoscope. Yet this patient had metastatic glands. When the epithelioma of the lip has involved bone I have not a record of an accomplished cure, even after the most extensive dissection.

Upper Lip.—With the exception of four cases the lesion was situated on the skin and was either a basal-cell epithelioma or a malignant wart. Local excision accomplished a cure. In the spinal-cell tumor the same operation should be performed as when the tumor is situated on the lower lip. The differential diagnosis, therefore, is important.

Face and Cheek.—The majority of lesions here are of the basal-cell type, but the tumor must be differentiated from the less-frequent spinal-cell carcinoma, because in the latter, if a larger local operation combined with the glandular dissection is not performed, there will be no hope of a permanent cure.

On the chin, eyelid, ear and nose the problem is the same as on the face and cheek; here also the less malignant basal-cell tumor is more frequent. But if the tumor is of the spinal-cell type the local operation must

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be more extensive, and, my experience teaches me, also combined with glandular dissection.

Scalp and Forehead.—The local operation is apparently sufficient in early cases for all types of tumor. In the spinal-cell tumor one should also remove the pericranium, and, if this is apparently involved, some bone.

Mucous Membrane of Gum, Mouth, Hard Palate.—The relation between carcinoma and chronic inflammation is illustrated in the study of these cases. Up to the present time I have never observed a carcinoma of the mucous membrane of the gum, except about decayed teeth or the root of an old, partially extracted tooth. The lesion is less frequent on the mucous membrane of the cheek, and such patients have given a history of injury from a ragged tooth. With the rarest exceptions, the tumor is of the malignant type. Benign and malignant warts have been observed only on the hard palate. The basal-cell tumors are so infrequent that they can be practically excluded. A very extensive operation offers the only possible hope of a cure. The ulcer must be removed with a wide zone of healthy mucous membrane and bone, and with this local operation there must be *en bloc* removal of the tissues extending to and including the neighboring lymphatics.

Tongue.—The surgery of malignant epidermal tumors of the tongue is a chapter by itself, and I shall not take space to discuss it here. The surgeon, however, must be on the lookout not to mutilate individuals with tubercular or syphilitic ulcers, with benign or malignant warts, or with basal-cell epithelioma by the radical operation indicated in carcinoma spinocellulare. This undoubtedly is the most common lesion as shown in the table, but the other possibilities enumerated must be borne in mind. I have also observed other benign lesions of the tongue—a fibroma, a blood cyst and a small lymphangioma.

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I have examples of every one of the benign types in which too radical a procedure has been performed for one of these lesions, because the correct diagnosis was not made as it should have been. To-day surgeons rarely are given an oportunity to operate early for cancer of the tongue. The individual naturally dreads the loss of his tongue, and many physicians and surgeons, fearing perhaps a mistaken diagnosis, wait until the protruding tongue has cancer written all over it.

If the public and the profession could be confident that the extensive operation would be performed for cancer only, and that the differential diagnosis is not difficult, even in the early stages, I am convinced that we would get the cases earlier. The patient should also know that the mutilation of the most extensive, well-planned operation is never as distressing as the disease when left alone. I am surprised to find in the few cured patients whom I have observed that in every instance bone was removed in order to permit a better dissection of the floor of the mouth. Except in one of my own cases, the bone of the lower jaw was not excised deliberately, but because of the local extent of the disease. Yet, a few of these patients have been permanently cured while in earlier, more favorable cases patients have died of local recurrence, because the apparently confined local growth had influenced the surgeon against the more mutilating extensive operation. My investigation is not yet complete, but the evidence thus far demonstrates that in the past surgeons have taken too much tongue, more than enough glands of the neck, but have restricted their operation as regards the floor of the mouth. If sufficient of the floor of the mouth is removed without including a piece of the lower jaw, it is impossible to close the mouth, and the danger of pneumonia is very great. It is my opinion, therefore, that the future operation for carcinoma of the tongue will either be the removal of the tumor only in those cases in which

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we get the lesion within a few days, or, a most radical local operation in which, in addition to a sufficient area of the tongue, the entire floor of the mouth of the area involved, with a piece of the lower jaw, is removed *en bloc* and combined with dissection of the glands of the neck. I trust to be able in the near future to have evidence which will make this statement more convincing.

The lesions of the *skin of the neck, body, upper and lower extremities may be considered together.* The problems are apparently identical. As to why carcinoma spinocellulare is so frequently observed at the mucocutaneous border of the lower lip, and in the tongue, we seem to have no definite explanation. It is difficult to bring together cause and effect. In carcinoma of the gum the cause stands out prominently. The frequency of basal-cell epithelioma on the face, cheek, chin, eyelid, ear and nose may be explained by the fact that these basal-cell tumors are of congenital origin, or that they are acquired later in life on account of the exposure of these parts. In the skin of the body and extremities basal-cell tumors are less frequent, but we rarely see malignant epithelial tumors of the areas just mentioned without the history of a wart, of a wound or ulcer, or of some chronic inflammation of the skin, eczema, psoriasis, *x*-ray burn, etc. Here carcinoma never begins with the same spontaneity as apparently happens in the lower lip and tongue. There is therefore a distinct precancerous lesion which can and should be eradicated in that stage. When the fully developed tumor presents itself surgeons should not be content with the restricted operation of the past. For carcinoma spinocellulare in its fully developed ulcerous or fungous state the operation should be along the lines employed in the breast; a wide area of skin, a broader area of subcutaneous fat, fascia always in some cases muscle, and always the neighboring lymphatics. There may be

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cases in which infiltration of bone will be encountered, indicating amputation.

The surgical treatment of carcinoma and sarcoma of the extremities emphasizes the deplorable fact that surgeons have had a wrong notion of the local growth of these two neoplasms; for sarcoma amputation has been the rule, while for carcinoma a less radical operation has been performed. As a matter of fact the reverse should be the rule. But this is not a question for the dermatologist.

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TREATMENT OF MALIGNANT GROWTH OF THE SKIN FROM A DERMATOLOGIC STANDPOINT

WILLIAM ALLEN PUSEY
CHICAGO

In considering the treatment of malignant diseases of the skin from the dermatologist's standpoint, the topic assigned to me, I shall take up only cutaneous carcinoma. I shall use the term "epithelioma" as synonymous with primary carcinoma of the skin and shall make no distinction in principles of treatment between rodent ulcer and squamous epithelioma confined to the skin.

The successful treatment of carcinoma of the skin, as of other tissues, requires, in the present state of our knowledge, the complete local destruction of the growth. The future holds out possibilities for the relief of carcinoma by systemic treatment, but at present we have no systemic methods that have any definite effect on the course of carcinoma. None of the agents used empirically has proved of value, and the agents which have been assumed to have a rational foundation, as cancroin, the cancer serums, and trypsin, have all proved totally useless.

INTERNAL REMEDIES

The only one of the internal remedies that seems to be entitled to the slightest consideration for its claims even to inhibit the growth of cancinoma, is arsenic. Arsenic, administered in large doses, undoubtedly has a definite effect on the nutrition or growth of the skin,

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and equally certainly some cases of sarcoma of the skin have been cured by the persistent and usually heroic use of arsenic. Some very careful observers, as Sherwell, and Abraham Jacobi, believe it is of benefit in carcinoma, and I believe when we are taking stock of our remedies for carcinoma, arsenic is entitled to mention as having a possible effect on the course of the disease—an effect not radical, but inhibitory.

We then are compelled to face the fact that the only way we can treat carcinoma successfully is to destroy it locally; and the practical question is, How can this best be done.

Obviously there are many ways in which living diseased tissues can be destroyed, and there are a number of methods of destroying cancinomatous tissue which are available for therapeutic application.

EXCISION

The most popular method and the one of preference among surgeons is excision. Excision is the only method practicable in many carcinomas, as those of the internal structures of the body, and in such situations we must avail ourselves of the one resort we have. But there are broad objections in principle to excision in carcinoma. In a large sense it is the crudest method of treatment. It removes an entire part, in the hope of removing with it diseased tissues which form only a fraction of the whole. It takes no account of the ability of the tissues to assist in the defense against carcinoma. A clean excision, healing practically without inflammatory reaction, must remove every cell of carcinoma to be successful. If it fails in this, no reaction has been excited in the tissues that may destroy remnants of the disease, on the contrary, lymphatic spaces have been opened up, and other opportunities given for the more favorable growth of any part of the carcinoma left. So, if clean excision fail in absolute removal *en masse*, the procedure has shot its one and only bolt, and the disease remains.

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These are not the objections of one opposed to operations in carcinoma; they are inherent difficulties in the principle of teatment of carcinoma by aseptic excision which if they could be avoided in all cases, would simplify the problem of successful treatment. Surgery recognizes these difficulties in constantly devising more radical and still more radical operations. It also recognizes the great danger of clean incisions which go into carcinomas, whether through the body of them, or through the peripheral offshoots. Thus Meller[1] in a statistical study of the result of surgical treatment in carcinoma of the head, neck, and face in Hochenegg's clinic in Vienna observes that local recurrence in and about the scar (after operation for cancer of the lip) is very much more frequent than glandular recurrence; which is another way of saying that the greatest difficulty in operative removal is to get all of the local growth. From the study of this series of cases he also calls attention to the often observed fact that operations which are not complete hasten the fatal termination of the disease by favoring extension along the opened channels and in the mutilated tissues. And he concludes: "May these figures be a warning to all those who face this disease without sufficient equipment; the knife of the unpracticed, untrained surgeon does more harm than good."

These facts are, of course, well known, and the statements from Meller are not quoted for themselves, but because of the corollary to them. The corollary is that: the dangers that arise from clean excisions in and about carcinomas should be avoided when the complete destruction of the carcinomatous mass is possible without resorting to such procedure.

Again, W. S. Halstead, in writing on the operative treatment of carcinoma of the breast, emphasizes the danger of incisions into carcinoma, even for material for diagnostic examination, as follows:

1. Meller: Ztschr. f. Krebsforsch, 1907, p. 64; reviewed editorially in THE JOURNAL A. M. A., Nov. 16, 1907, xlix, 1677.

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It was my practice at one time in making the exploration in doubtful cases to excise a portion of the breast tumor with the Paquelin cautery to prevent the wound inoculation which I feared might take place if the knife were used. The excision of a specimen for macroscopic or microscopic examination is never resorted to except just before operation. If the actual cautery for any reason is not used the wound is immediately cauterized with carbolic acid. All incomplete operations for cancer should, when feasible, be made with the Paquelin or actual cautery.[2]

These dangers from the use of the knife obtain with equal force in carcinoma of the skin, in which, especially on account of the necessity of sacrificing as little tissue as possible, there is often presented a difficult problem in getting beyond the borders of a growth. To put it in another way, if it is dangerous to cut into a carcinoma, why should excision without cauterization be the method of preference in epitheliomas in which one usually is compelled to save as much healthy tissue as possible, and often cannot be sure whether his knife has gone through carcinomatous tissue or not?

OTHER METHODS OF DESTRUCTION

This brings us to the question, are there any available methods for destroying carcinomas other than excision? As I have already said, for internal carcinomas there are none; for carcinomas of the skin there are several which compel consideration by the open mind.

Let me say at the outset that I would exclude from consideration among non-excision methods all measures which are not vigorously destructive. Superficial caustics, like silver nitrate and phenol, are dangerous. They do not cause deep destruction of tissue themselves, nor do they produce a reaction sufficiently intense to destroy carcinomatous tissue, and, like all other irritants which fall short of destruction, they tend to make

2. "I was greatly pleased to note during a visit to Rochester, Minn., that Drs. William and Charles Mayo make extensive use of the actual cautery in operations on cancers incurable by the knife, and to have them indorse the view, so long maintained by me, that there is relative immunity from local metastasis with the employment of the cautery." W. S. Halstead: Tr. Am. Surg. Assn., 1907, xxv, 61.

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the growth more rapid. Equally ineffective for curative purposes are substances like pyoktanin, which promote epidermization and healing of ulcerated surfaces; they are especially dangerous in inexperienced hands, because the deceptive healing of the surfaces which they promote may be regarded as evidence of cure and valuable time thus be lost in making the radical attack.

The attempt to treat cutaneous carcinoma by high-frequency sparks or brush discharges, in the way this treatment is carried out in epithelioma, should also be included among the less vigorous and effective methods; it is not a method of treatment by actinic energy, like radiotherapy, and, when used with sufficient intensity to be effective, is a very awkward and painful way of doing a simple thing. In the same group of ineffective methods I would include simple currettage, no matter how vigorously done, and, except in cases most carefully selected by men of large experience, electrolysis and the new method of refrigeration, either with liquid air or with solid carbon dioxid.

Electrolysis, which is occasionally used for treating minute epitheliomas, does not destroy the tissue in sufficiently large masses to be a desirable method of treatment.

Refrigeration by liquid air or solid carbon dioxid, because of its ease of application and relative painlessness, is useful in very superficial rodent ulcers; but neither liquid air nor solid carbon dioxid is sufficiently destructive to rely on without great care, and they should only be used, if at all, in carefully selected cases; which is another way of saying that they should be used only by one who is thoroughly familiar with what he is doing.

CAUSTICS

There still remains a group of agents which, experience has shown, are vigorously destructive of carcinomas. These are the strong chemical caustics, like caustic potash, zinc chlorid, arsenous acid, and the strong

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minerals acids, the actual cautery and highly actinic forms of radiant energy in the form of Röntgen rays and radium rays.

The advantage which comes from the use of strong caustics, like potassium hydroxid, in treating carcinoma is that one is using an agent which not only promptly destroys the cancer tissue into which it penetrates, but at the same time blocks lymph-channels, and produces a violent inflammatory reaction that extends widely beyond the area actually destroyed—a reaction that offers a good prospect of destroying outlying diseased cells and that builds up a strong barrier of inflammatory connective tissue. A. R. Robinson[3] has for years insisted on the usefulness of caustics in cutaneous epithelioma; and it is but fair to quote his description of the reasons why they are advantageous in the treatment of these lesions.

HOW CAUSTICS ACT

For the purpose of simplicity and clearness of description Robinson assumes that an epithelioma may be divided into three zones: a central area, A, which represents the epithelioma visible to the naked eye; around A a zone, B, in which carcinoma cells exist, but are not macroscopically evident; around this a third zone, C, in which perhaps some carcinoma cells exist, but beyond whose outer border it is highly unlikely that the disease has extended. Then describing the effect on an epithelioma of a caustic such as arsenous acid, he says:

All of the tissue within A has been destroyed, deprived of its vitality, and also some of the tissue beyond A on account of the very intense inflammatory process there, the tissue being much more vulnerable than normal tissue on account of the injury received from the epithelial invasion; hence the completely necrosed tissue always appears to embrace a larger area than the epithelioma seemed to occupy when seen by the naked eye. Beyond this completely necrosed area the inflammatory process becomes less and less intense the less the tissue is invaded by the epithelial cells, but if the caustic has been

3. Robinson: Med. Rec., New York, March 31, 1900, p. 355.

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applied for a long period the inflammation will be sufficiently intense to destroy all pathologic epithelia as far as B, and almost without exception as far as C; that is, the disease is removed as completely as if the incision by the knife had been made at C, although the normal tissue has been destroyed not even as far as B. Of course the favorable action extends in depth as well as outward in all directions from a center. The proof that the outlying epithelial cells are destroyed consists in the fact that the disease rarely reappears after such a condition of necrosis and inflammation has been produced.

The destruction of these outlying cells depends, in my opinion, first, on the existence of the acute inflammatory process destroying the pathologic tissue quicker than it does normal tissue, according to a general law in pathology, and especially so in this instance, as the pathologic epithelia lie in the lymph-spaces and can, therefore, be vigorously acted upon by the inflammatory lymph, thus changing quickly and very greatly the previous condition under which they lived. . . .

To repeat somewhat: from the proper action of this caustic, the same result as regards removal of the disease is obtained as if all the tissue within C had been removed by the knife, although normal tissue has been taken from a less area than that included within B; that is, that the caustic is in suitable cases a much more conservative agent than the knife, and therefore it should be employed in all cases in which it is an efficient one and deformity is to be avoided as much as possible, as in all face cases, for example, especially in cases of nose epithelioma. It must not be forgotten also that this method of treatment enables the surgeon to destroy the sometimes deep-lying cancerous tissue that cannot be excised for some reason or other.

In conclusion he calls attention to the fact that it is not desirable for these wounds to remain aseptic, but that the usual moderate infection from the pus organisms of the skin aids in making the inflammatory process more intense, and of longer duration, and stimulates the growth of the granulations which are of benefit in lessening deformity.

That the theoretical advantages to which Robinson calls attention do actually exist, and are of practical benefit in the treatment of epitheliomas which are amenable to caustic treatment, has, I believe, been shown to those who are familiar with the results obtained with these methods of treatment. The scarring which

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results in these cases, when the treatment is carried out by experienced hands, is relatively very slight in proportion to the amount of destruction of tissue that may be required, and the results, I am convinced, will bear favorable comparison as regards permanency with the results of the treatment of similar lesions by clean excision. The impression as to the radical character of the results of caustics in carcinomas involving superficial structures, is not confined to dermatologists. Note, for example, the following quotation in regard to the treatment of carcinoma of the breast with caustics:

> **I am indubitably convinced that the local and regionary recurrences after incomplete operation, which come, as a rule, with amazing rapidity when the knife has been used, are, to say the least, relatively late in making their appearance when chemical or actual cautery has been employed. I have several times had occasion to operate on cancers which had been vigorously and repeatedly treated with caustics, and to note the relatively admirable condition, the freedom from cancer permeation of the surrounding tissues and of the axilla; whereas, after incomplete operation with the knife the local manifestations of recurrence were almost invariably deplorable and the prognosis, of course, invariably hopeless.**

This statement of the excellent character of the results of caustics in carcinoma tissue it not from a dermatologist, but from one of the foremost authorities on the operative treatment of carcinoma—Dr. William S. Halsted. The favorable effects of caustics on carcinoma, which he summarizes so admirably, apply with especial force in the treatment of localized carcinoma of the skin. I have had occasion, in a few cases, to observe the results from the use of caustics in the total removal of the breast, in one case, of both breasts, and I can confirm Dr. Halsted's statement as to their character. They fully bear out the claims made by Dr. Robinson, as to the radical effects of caustic treatment, when thoroughly applied in the treatment of carcinoma. I have also had occasion to see surprising radical results in extensive epitheliomas, which had failed of surgical cure, and were apparently beyond check. The man,

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like myself, who is called on to see the late cases of carcinoma in patients who have sought all sorts of methods of relief, regular and irregular, cannot but be impressed with the value of caustics, sometimes in the hands of irregular practitioners; and to feel the misfortune that surgery, as a rule, has not been able to keep an open mind in judging of treatment by caustics, with the result that their use has been left largely to irregular practitioners, most of whom are ignorant and who do much harm, but who, inspite of this, occasionally produce with caustics amazing results in cases which have been signal surgical failures.

CHOICE OF CAUSTICS

The choice of chemical caustics for the treatment of epitheliomas lies practically between arsenous acid, zinc chlorid, caustic potash and acid nitrate of mercury. Robinson prefers, as a rule, arsenous acid; Van Harlingen, caustic potash; Sherwell, acid nitrate of mercury. All of these are agents which totally destroy cancer tissue with which they come in contact, and all, except arsenous acid; produce immediate destruction of healthy as well as diseased tissue. Arsenous acid, in proportion of 50 to 75 per cent., with powdered acacia 50 to 25 per cent., mixed with water to form a paste, requires for the destruction of a mass of superficial carcinoma of the skin from six to twenty-four hours. It may be said to possess some selective action in the destruction of carcinomatous tissue. The others progressively destroy all tissues with which they come in contact and require for the destruction of an epithelioma an application of only a few minutes' duration—from five to twenty. The technic of the application of these agents, into which I cannot go fully here, is easily available in the detailed writings of Robinson, Sherwell, Van Harlingen, Gottheil and others. The successful treatment of epitheliomas with caustics requires knowledge of the methods, and one should familiarize himself

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with these methods before undertaking to use them. In the use of caustics, as in operative procedure, knowledge and judgment are needed. No one method is applicable to all cases and no one technic. In the use of a caustic there is required the exercise of judgment and the adaptation of means to ends, quite as definitely as they are demanded in treatment by excision.

THE RÖNTGEN RAY

No one who is not blind to facts can doubt, if he will take the trouble to investigate, that carcinomatous tissue in the skin can be destroyed with *x*-rays. On the basis of a large experience in primary and secondary carcinomas of the skin, I am willing to maintain that carcinoma tissue in the skin can be destroyed by exposure to *x*-rays as certainly as by any mechanical or chemical method; that the method, therefore, can be used with assurance, and that the results as regards permanency are fully as good as those obtained by any other methods. There are certain theoretical advantages which the use of the *x*-ray offers over other destructive methods.

First.—It is painless and avoids the ordeal of operation. This is an advantage not only of humane consideration, but of practical importance, because it enables one to treat early lesions in cases in which the patient will not at the time accept the gravity of the situation and submit to operation or any other method of gross destruction.

Second.—The method may be so used as to destroy carcinoma cells, but leave in large part the connective tissue stroma intact and in condition to repair itself.

Third.—Accordingly it leaves small scars.

Fourth.—It can be used in cases in which the surrounding healthy tissue cannot be sacrificed. This means that:

Fifth.—It is valuable in certain cases in which ordinary methods are objectionable, because they involve extensive operations and serious subsequent disfigurement, as, for example, about the eye and nose. This means further that:

Sixth.—It has a field of usefulness in some cases in which ordinary methods are impossible, because of the amount of destruction of tissues which complete removal would require;

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in other words, it may be used to produce a radical result in some inoperable cases and to improve and inhibit the course of other inoperable cases.

These theoretical advantages of the use of *x*-rays are a practically verbatim quotation of a statement of mine published seven years ago, and my subsequent experience confirms me in the belief that their accuracy has been established by practical results.

I have written so much on the use of *x*-rays in epithelioma that I do not feel that I should impose on your patience by an extensive consideration of this subject on this occasion. In brief, I may say that except in those cases which I think are properly treated only by excision and a radical surgical operation, to be considered later, treatment by *x*-rays is my method of preference in epithelioma. As a rule, but not always, the method is slower in results than the older methods, but this is its one disadvantage. As to the radical character of the results, they may court comparison with any other method of treatment. In a paper read before the Sixth International Dermatological Congress in September, 1907, I gave a detailed report of the results in 111 consecutive cases which had been treated three years or more before. In this list there were 72 per cent. of successful results; of the patients not incurable by other methods, practically 100 per cent. were successfully treated. Without entering into statistical considerations here, I believe I may say fairly that in an experience now numbering hundreds of cases of epithelioma treated with *x*-rays, I have not had occasion to regret that I had used *x*-rays; and I say this with, I trust, a fair appreciation of the results obtained in the treatment of epitheliomas by other methods. The disappointments at failure radically to relieve operative epitheliomas by treatment with *x*-rays have been very few. I have had a very much larger number of disappointments at failure greatly to benefit hopeless cases. Nevertheless, the most valuable use, perhaps, of *x*-rays in carcinomas of the skin is seen in

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the palliation and temporary relief of the cases which are hopeless of other benefit.

I trust I may be pardoned for basing my remarks on the use or Röntgen rays in carcinoma solely on my personal experience, on the ground that in a comparatively new field, like the use of Röntgen rays in carcinoma, one can speak with the most assurance from his own experience.

Excellent results in cutaneous carcinomas have been obtained by F. H. Williams, Abbe, Wickham, and others with radium. In a previous paper I have indicated my belief that there is no essential difference in the form of energy concerned in treating epitheliomas with radium and with Röntgen rays. I know of no results obtained with radium which have not been duplicated with Röntgen rays, and in my opinion there is little ground for choice between the two methods. The obstacles to the use of radium lie in the difficulty in obtaining it and the fact that it exists in such small quantities that it is impossible to obtain more than a minute fraction of the quantity of actinic energy which is furnished by the ordinary *x*-ray apparatus.

COMPARISON OF METHODS

In referring to the comparative advantages of different methods of treatment in cutaneous carcinoma, I would emphasize as strongly as possible the importance of a sharp line of distinction between the cases which are suitable for treatment with caustics or *x*-rays and those which should be treated by excision. I would make no distinction on their histologic structure—between squamous-cell epitheliomas, which are apt to be deeper, and the superficial lesions of the rodent ulcer type, the so-called basal-cell carcinomas of the skin. I do this fully understanding that there is often a marked difference in the clinical course of rodent ulcers and alveolar epitheliomas, but I am, nevertheless, fully convinced that the treatment of rodent ulcers should be carried out on exactly the same principles and as vigor-

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ously as that of other carcinomas of the skin; that they occasionally have metastases; and that if left untreated or treated badly, while they will likely pursue a slower course, from that very fact they often cause more disfigurement and more suffering than more rapidly growing carcinomas.

For the purpose of treatment, I divide epitheliomas into two classes: First, those in which rational treatment requires only the complete destruction of the growth *in loco;* second, those in which rational treatment requires removal of contiguous glands, or—having in mind in this connection the orbit—the deep removal of underlying tissue.

In the first group of cases—those in which treatment requires only the destruction of the growth in its primary location—I believe that as a rule the *x*-ray is the best method of treatment; that after that the use either of a caustic or of a mechanical method of procedure, like curettage, always to be followed by a strong caustic, is the second method of preference. This condition, the necessity for the removal of contiguous glands, eliminates from this method of treatment, most lesions occurring on the mucocutaneous junctures. It requires that the most epitheliomas occurring at the anus, and on the penis and scrotum, and perhaps most epitheliomas occurring on the vulva, should be immediately submitted to radical operations. Perhaps there are some cases of epithelioma about the external genitals which do not require a radical operation, but my experience is so small in all but late epitheliomas of the external genitals that I should want some one of wider experience than myself to decide before I would undertake the treatment of any epithelioma of these parts by its local destruction. This condition also demands a radical surgical operation for most epitheliomas of the lower lip—not of the skin surface of the upper lip—but it is indubitably true that there is a type of superficial epithelioma of the lip which the expert can recog-

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nize as such, and whose radical cure does not require the removal of the glands beneath the jaw. These lesions are very superficial epitheliomas, usually occurring in old people and perhaps lasting for years without deep involvement of the lip. They begin in most cases—I am not sure not in all—in patches of hypokeratosis or of leukoplakia of the lip. These, after continuing without manifestations of irritation for years, perhaps finally show an irritated base with some excoriation of the surface, and then there is slow progression along the surface of the lip. I have treated perhaps forty consecutive cases of this sort, most of them referred by surgeons, without a single development of carcinoma in the lymphatic nodes of the neck.

But the selection of the treatment applicable to these cases requires the greatest caution, and their treatment should not be undertaken unless one fully understands what he is doing. Because of the danger of the abuse of any method of treatment of epithelioma of the lip which does not involve the removal of the glands beneath the jaw, I should be glad not to mention the practicability of the treatment of any epithelioma of the lower lip by methods of local destruction, were it not for the fact that there are some cases in which this less radical procedure is highly desirable or the only resort possible. There are other situations in which the decision of the question as to the removal of the contiguous glands requires the exercise of mature judgment; but it is in epitheliomas of the anus, of the external genitals, and of the lower lip that this question is of most importance. In the treatment of epitheliomas about the eye the question of attacking the orbit surgically arises. In lesions beginning on the upper or lower lids, involvement of the orbital tissue is slow to occur and the *x*-ray offers the ideal method of treatment. When epithelioma palpably involves the orbital tissues, the radical cleaning out of the orbit is indicated. This danger is greatest with epitheliomas occurring near

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the inner canthus, and in such cases local destruction should be undertaken with the utmost caution. Lesions occurring on the temples and near the outer canthi do not nearly so frequently call for destruction of the eye by radical operation, and are often amenable to treatment with *x*-rays.

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ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. LOEB, FORDYCE, MALLORY, BLOODGOOD AND PUSEY, CONSTITUTING A SYMPOSIUM ON CANCER

DR. E. R. LECOUNT, Chicago: There seems to be a subsidence of belief in the parasitic origin of tumors and a diminution during the last few years of investigations to find such parasites. The prevalence of the former belief in a parasitic origin of tumors may be accounted for by the conspicuous place which the infectious diseases occupied in investigative medicine during the last few decades. With the lessening of search for a "cancer parasite," opportunity has been offered for researches in other directions. In general these have been of two sorts, one of them the old and well-worn subject of the histogenesis of tumors, still capable of yielding valuable information; the other, the newer study of transplantable spontaneous tumors of animals. In regard to the last of these, the results have been the development of a new branch of medical literature, new journals and the founding of special institutions by both private and public funds. Some of the articles dealing with phases of tumor transplantation are as difficult for the average physician to comprehend as many of the contributions to the problems of immunity. In both fields of investigation there is a great deal which needs collating for the physician with average equipment. In general the results which have so far occurred from study of these transplantable tumors are: 1. Learning that only a relatively small percentage of the transplantations lead to successful growing grafts. 2. The belief in a continuity of tissue growth —that all the successful grafts represent direct ancestry of the tumor with which the experiments began. 3. The undoubted experimental production of a malignant tumor which has been observed a few times when metamorphosis of a carcinoma into sarcoma has taken place. 4. The altered tactics among these investigators very recently in now attempting to modify, control or prevent processes of tumor growth which they are able to bring about; in other words, to produce an immunity. 5. The gradually growing suspicion, now almost a conviction in the minds of some, that the growth of malignant tumors is largely depend-

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ent on processes of metabolism not understood at present, but which may eventually be found analagous to those which are concerned with normal growth.

Dr. F. B. Mallory, Boston: I should like to say a word in connection with the paper of Dr. Fordyce in regard to epidermoid carcinomata. In the ordinary epidermoid carcinoma the cells differentiate like those of the epidermis. The cells of the rete Malpighii are cubical to cylindrical in shape and have considerable cytoplasm. These cells show a slight fibrillation of the cuticle. In the prickle-cell layer the fibril formation is much more marked. The fibrils are numerous and short. Finaly the cells undergo a hemogenous transformation with cornification which leads in the tumor to the formation of the so called epithelial pearls. In the non-cornifying type of carcinoma of the skin, the so-called carcinoma baso-cellulare, the cells vary from cubical to spindle in shape, have little cytoplasm and do not lead to prickle-cell formation. Instead these cells often produce numerous very definite straight and wavy fibrils of considerable length. The only cells in the skin which differentiate in this way are the cells leading to the formation of a hair shaft. These cells are spindle in shape, have little cytoplasm and produce numerous long, wavy fibrils which gradually undergo a homogenous transformation and form the shaft of the hair. Judging from the cell differentiation which they undergo this type of tumor arises from the hair matrix.

Dr. J. W. Vaughan, Detroit: It is interesting to note that the results of the treatment with the *x*-ray in some cases are apparently far superior to the use of purely surgical measures. I will attempt to give a possible explanation for this fact. The late Dr. Hodenpyl of New York, cured a cancer of the liver by the use of injections of ascitic fluid; the ascitic fluid gave good results in other cases. In addition to that we have the work of the experimenter who injected a suspension of cancerous cells into patients with beneficial results. In my own experiments I split up the cancer cells with a 2 per cent. solution of sodium hydrate in absolute alcohol. The non-toxic residue is insoluble, and I injected this portion with apparently beneficial results. Now, how does this apply to the better results we get with the *x*-ray, as compared to purely surgical measures? If you take cancer tissue and expose it to the *x*-ray for fifteen minutes it splits up the cancer tissue the same as the caustic sodium hydrate solution, into its toxic and non-toxic portions. The good results following the use of the *x*-rays, I believe, are due to the fact that the rays form an active ferment within the body of the patient, which in itself splits up the cancer cell, and is not due wholly to the destruction of the cancer cell.

Dr. Willy Meyer, New York: In the treatment of skin affections by radium it is necessary, in the first place, to have

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radium of great strength. The application and treatment is comparatively simple and nothing that I know of can be compared to the results obtained by it. In cases of tumor of the skin, warts, epitheliomas, etc., Dr. Abbe proposes to make these radium applications for a period of half an hour and then send the patient away. I have obtained good results by using it in such cases at close range for five minutes the first day, adding to this time one minute for three successive days, and then on the fifth day allowing the radium rays to exert their effect on the immediate surroundings of the tumor for ten minutes. Then the patient is sent away and is not seen again for three or four weeks. By this method, in three different cases, I have seen the marvellous effects of radium, similar to those described by Dr. Abbe in his oration on surgery at this session. The patients with what we formerly called epithelioma or rodent ulcer, especially when located about the nose and eyes, where they are unusually disfiguring, come back to us after this method of treatment with a scar which, while it is somewhat below the level of the skin, remains a healthy scar, without showing any evidence of recurrence. In one of my cases two years have now elapsed without a recurrence; in two others the interval is shorter. There is nothing, in my experience, that can be compared with the wonderful effect of this method of treatment, which often acts where the *x*-ray fails. The only drawback is that radium is very scarce and very expensive. It is to be hoped that pitchblend will soon be found in large quantities in one of the many mines of our country. In that case I am sure dermatologists would be the first to make more frequent use of this apparently wonderful remedy.

Dr. William T. Corlett, Cleveland: I believe that the ideal treatment for cancer is not yet known. During the last twenty-five years I have worked with my colleagues, the surgeons, in handling many cases of cancer, and I believe if one acts honestly and studies his cases well he will not adopt any one method of treatment to the entire exclusion of others. The main thing that has been brought out in the discussion thus far in the treatment of cancer is the early eradication of the disease. The method of this eradication, I believe, is of secondary importance, but it is the early recognition and thorough eradication that is followed by the best results. Everybody who sees many of these cases must be impressed with the fact that many patients are allowed to go on for months and years, receiving only dilatory or insufficient treatment, until the case is beyond the scope of operative measures. Every clinician must have observed, too, that there are different degrees of malignancy, as has been pointed out in the histologic presentation. There are cases of cancer of the skin in which the knife is the only means that can be employed, but in many cases the knife is not the best means. When it is, it

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is advisable in many instances to follow it by a thorough course of *x*-ray treatment. In regard to the use of caustics, we are familiar with the work of Robinson, and, while I have had little personal experience with caustics, I believe they are effective and in selected cases are good. One objection to them is that they are painful, and personally I believe in most instances there are better methods. The Roentgen ray in some cases is the best and only method, and in others the knife is not only the best but the only method. The Roentgen ray, I believe, is not the most efficient, for after this method of treatment only a certain number will remain free from the disease for a period of years. The method that I have adopted very largely for at least twenty-five years at the Lakeside Hospital is electrolysis. Of late this method has received attention by Brocq of Paris, and some Germans have spoken of it favorably. When I first adopted this procedure I did it at the request of the surgeons in cases in which the use of the knife was not deemed advisable. In these cases and in many others since then the results have frequently surprised me. They have been very favorable, and I hope some time in the near future to present a tabulated report of my results. That the procedure is indefinite, as stated by Dr. Pusey, I refuse to concede. My method is to introduce both electrodes around the malignant growth, penning it in, and afterward to introduce them into the growth itself. It is advisable, I believe, to go beyond the margin of the growth and produce a decided reaction. Many of these patients, to my personal knowledge, have gone from nine to fifteen years without a recurrence; others have died of old age, but I have no detailed statistics to present at this time. Finally, the method to be selected in the treatment of cancers of the skin should depend on the nature of the case. In some the knife is best, in others the Roentgen ray, while in suitable cases, before metastases have occurred, electrolysis is followed by excellent results. Of course, where glandular involvement has already taken place, it should not be considered; then the knife is imperative.

DR. A. RAVOGLI, Cincinnati: I was very glad to hear Dr. Mallory speak of the possibility of micro-organisms finding an entrance through the opening of the sebaceous glands, and to listen to Dr. Fordyce's remarks regarding the precancerous changes in the skin and the development of epitheliomas on certain dermatoses; that it was possible that a micro-organism might be the cause of this preceding disease of the skin, and then the causation of the cancerous changes. I have always believed in the parasitic origin of cancer, and still incline to that view. The success of the transplantation experiments, I think, point to the correctness of that theory. There must be something which produces the changes and the proliferation of the cells. As regards treatment, I find that formalin gives me very good results in superficial epithelioma and carcinoma.

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My usual procedure is to curette the lesion and then apply a 40 per cent. solution of formalin. The pain that this method gives rise to can be allayed by a 5 per cent. solution of cocain. After two or three days the surface of the lesion begins to harden into a whitish or yellowish eschar, and when this falls off, a second application is rarely necessary. I have had a large number of these cases, perhaps 40 or 50, where my results with formalin have been very satisfactory. I also wish to mention the use of Coley's fluid, especially in fibrosarcoma. I have seen cases in which the growths were so extensive as to be practically inoperable improve under the injections of the streptococcus erysipelatis and bacillus prodigiosus, as advised by Dr. Coley, and I think this remedy should be borne in mind in extensive cases that are not amenable to other methods of treatment.

DR. J. A. FORDYCE, New York: I was very much interested in what Dr. Mallory said in regard to the infiltrating angioma. This seems to bring it into connection with the angiosarcoma of Kaposi.

DR. WILLIAM A. PUSEY, Chicago: I am glad to see from this discussion that we are not so far apart in our views on this subject. I think the consensus of our views is that the proper treatment of carcinoma is to destroy it. It does not make so much difference how you do it, providing you do it. For this purpose I prefer to use vigorous meaures. I do not like formalin nor pyrogallic acid. As to any antibodies or ferments being produced when you treat carcinoma with the *x*-ray, I have looked for such an effect as longingly as anybody, and I am compelled to say that I have seen no such effects. I have seen great masses of sarcoma and carcinoma disappear under the *x*-ray, but as far as my experience goes I have not been able to see a glimmer of hope that by this method of treatment any antibodies were formed that were of any value. We must depend on the destruction of the cells by the *x*-rays. As to the comparative value of radium and the *x*-ray, I believe that the results of these two agents are very similar and that in both instances we are using practically the same agent.

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RESULTS OF EXPERIENCE WITH NOGUCHI MODIFICATION OF THE WASSERMANN SERO-DIAGNOSIS TEST FOR SYPHILIS

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In selecting a method for the performance of the complement-fixation test of syphilitic sera, we were influenced by several factors, chief of which were the following:

In studying the different methods carefully and comparing the results obtained by different workers, we were impressed by the apparent accuracy of Noguchi's modification of the Wassermann test as shown by Noguchi[1], Fox[2], Swift[3], and others.

It was also much more convenient to secure human than sheep's blood for immunizing our rabbits and for the corpuscle suspension used in the test.

This paper is not intended to criticize any one method or to compare the efficiency of the different methods; but to give the results and conclusions drawn from the examination of four hundred and ten sera by Noguchi's method.

The majority of the patients were private patients of Drs. Hyde and Ormsby. The control specimens of syphilitic blood were secured from patients in Cook County Hospital.

Technic of the Test.—The technic employed was practically that originally recommended by Noguchi and described by him.

1. Noguchi: Serum Diagnosis of Syphilis, 1st Edition, 1910.
2. Fox: Jour. Cutan. Dis., xxvii, 338-357.
3. Swift: Arch. Int. Med., iv, pp. 376-404.

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A few minor changes were made in the method of securing some of the materials necessary for the test, but these had no relation to, and changed in no respect, the method of procedure in the test.

Five factors are employed in the test: antigen, complement, amboceptor, patient's serum, and human corpuscles.

Antigen.—The antigen used in this series was very kindly furnished by Dr. William T. Mefford, of Chicago. It was an alcoholic extract of a syphilitic liver and prepared by him. It was standardized by us according to the outline given by Noguchi.

Preparation of the Complement.—In the majority of cases, old guinea-pigs give the most satisfactory complement. I have found the most convenient and efficient method of securing the blood to be as follows:

The pig is anesthetized, the precordia shaved and sterilized and with a sterile syringe and needle sufficient blood for the test in hand is withdrawn from the heart. With a little practice and experience, difficulty is rarely encountered in piercing the heart with the needle. As much as 5 c.c. may be withdrawn from a good sized animal; from 5 to 10 c.c. N. NaCl are then injected into the peritoneal cavity in order that the vitality of the animal may remain at par. After the blood is withdrawn, it is permitted to clot at room temperature, the serum is removed with a pipette and placed in the ice box till ready for use. I never use a complement over thirty-six hours old.

The results in the earlier cases of this series clearly indicated that the sera of guinea-pigs varies greatly as to the amount of complement present. This undesirable feature was remedied in the following manner:

In securing the blood, as described, the life of the animal is spared and its health does not seem to be impaired. The serum from each animal is standardized according to Noguchi's directions as to the strength of the complement present; and after the first serum from each animal is tested, the additional labor of standardizing the complement every time a test is made, as suggested by Clark[4] is dispensed with. Furthermore, in private laboratories and in isolated districts where difficulty is encountered in securing guinea-pigs, it is very essential that the life of the animal be spared. Some of our guinea-pigs have been bled eight or ten times at intervals of three weeks, and the titer of the complement of each animal remains unchanged.

4. Clark: Jour. Infect. Dis., vii, p. 476.

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Preparation of Amboceptor.—A rabbit, preferably an old male, is immunized against human corpuscles as follows:

The blood from a normal individual is obtained by venipuncture from the arm, placed in sterile centrifuge tubes, defibrinated by stirring briskly with a piece of firm twisted wire. After being centrifuged the serum is removed with a pipette and the corpuscles washed with normal salt solution. After three washings, the supernatant NaCl solution being pipetted off each time, the suspension is made up with salt solution to the original amount of blood. It is then injected into the peritoneal cavity of a rabbit in increasing quantities and at intervals of five days, beginning with 3 c.c., then 6 c.c., 9 c.c., 12 c.c., 16 c.c., and lastly 20 c.c. Eight to ten days after the last injection, two or three c.c. of blood is withdrawn from the heart in the same way as when taken from the guinea pig, the animal being anesthetized. The serum is inactivated and tested as to its hemolytic properties as suggested and outlined by Noguchi. If the serum is found to contain an amboceptor of from .003 c.c. to .008 c.c. titer, 15 or 20 c.c. of blood are taken from the heart and immediately the same amount of salt solution is injected into the peritoneal cavity. At intervals of ten or twelve days, about 10 c.c. washed human corpuscles are injected into the rabbit. In this manner, an animal producing a good amboceptor can be kept indefinitely, and a fresh amboceptor of sufficient strength is always at hand.

Owing to the fact that so many rabbits after being injected are not satisfactory, it is very desirous that when we secure a good animal it be kept as long as possible. If after one series of injections the serum does not contain sufficient hemolytic properties, another series of injections may give a serum of the desired strength.

Blood to be Tested.—From 1.5 to 2 c.c. of the patient's blood is secured from the lobe of the ear, which has been properly cleansed. A puncture is made with a straight, three-cornered, sharp, surgeon's needle, which makes an opening sufficiently large so that the blood as a rule flows quite freely. It is collected in a glass tube that has been drawn out to a capillary point and bent in U-shape, the capillary arm being much the shorter. The small opening must be sufficiently large so that the lumen will not be occluded by the clotted blood before a sufficient quantity has been obtained. By making a good deep puncture, then gently squeezing the lobe, the drops are forced out; the capillary end of the tube is placed against the drop, which is drawn into the tube by capillary attraction. The tube should be held in the horizontal position. Difficulty is rarely experienced in getting sufficient blood in this way and it is

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usually less painful and disagreeable to the patient than when taken from the finger or by venepuncture. The specimen of blood is kept at room temperature for three or four hours, during which time the clot forms and the serum separates. The latter is withdrawn by a pipette, the rubber bulb on the pipette being perforated in order to control the serum better, inactivated by heating to 56° C. for thirty minutes and then placed in the icebox. It is advisable to make the test as soon as possible after the blood is procured. However, when the serum is inactivated and kept in a cool place it may be kept for several days. A strongly positive syphilitic serum was kept in the icebox several months with no impairment of its strength.

Suspension of Normal Corpuscles.—Two graduated centrifuge tubes are desirable in preparing the suspension. Into these is put a definite amount of normal salt solution. Blood is secured from the finger, a tourniquet having been applied and then the puncture made. The blood is permitted to drop into the tubes of salt solution in the proportion of one drop to 4 c.c. salt solution. The number of specimens to be tested will determine the number of drops to be drawn. The corpuscles are washed twice, after which the proper suspension is made. Two tubes are required for each serum to be tested, 1 c.c. of the quarter drop suspension being placed in each. A fresh suspension will usually give better results than corpuscles kept in the icebox for one or more days. Hemolysis is more complete in the control tubes and the contrast in a very mildly positive case more pronounced.

TABLE 1

	Tube number.	Inactivated serum, .08 c.c., 4 capillary drops.	Antigen, 1 unit.	Complement, 2 units.	Corpuscle suspension, 1 c.c., ¼ drop.	Amboceptor, 2 units.	Result.
Patients' serum.....	1	+	+	+	+	+	?
	2	+	0	+	+	+	Hemolysis
Positive syphilitic serum	3	+	+	+	+	+	No hemolysis
	4	+	0	+	+	+	Hemolysis
Normal serum.....	5	+	+	+	+	+	Hemolysis
	6	+	0	+	+	+	Hemolysis
	7	..	+(2)	+	+	+	Hemolysis
	8	..	..	+	+	+	Hemolysis

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After the material for the test is prepared an outline similar to that in Table 1 is used.

The tubes are numbered and arranged in a suitable rack or holder. One unit antigen, two units complement (usually from .03 to .04 c.c.), .08 c.c. of the inactivated patient's serum or four capillary drops are placed in tube 1. The same, with the exception of the antigen, which is omitted, is placed in tube 2. In tube 3 is the same amount of antigen, complement and corpuscle suspension, but positive syphilitic serum is added in place of the serum to be tested. Tube 4 is the same as tube 3, except that antigen is again omitted. Tube 5 contains normal serum with antigen, complement, and corpuscles. The antigen is again omitted in tube 6, the other material being the same. Tube 7 contains two units antigen, complement and corpuscles. Double the amount of antigen is added to this tube to see if it will inhibit hemolysis. Tube 8 contains complement and corpuscles. The tubes are shaken up well, then incubated for one hour at 37 C. Two units of amboceptor are then added to each tube and all the tubes are again incubated at the same temperature. Progress in the process of hemolysis should be closely observed. When hemolysis is complete in the control tubes, 2, 4, 5, 6, 7, and 8, and if there is complete inhibition to hemolysis in tube 3, the result in tube 1 is noted.

In part of the cases of this series additional control tubes were used, in some of which the complement was omitted, and in others the amboceptor was not added. But when the controls, as used in above table, are satisfactory, they seem to be amply sufficient.

The sera from fifty-two patients representing thirty-two diseases other than syphilis gave the results shown in Table 2.

The entire list was negative with the exception of one case of general paresis and seven cases of tabes which were positive; six cases of tabes being negative. There were also thirty cases of hypochondriacal syphilis and thirteen normal sera, all of which were negative.

In Table 3 are two hundred and ten cases in each of which is given the duration of infection, the type of lesion, if any was present, the treatment including both remote and recent, and the result of the test.

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TABLE 2.—DISEASES OTHER THAN SYPHILIS

Disease.	Number of Cases.	Result.	
		Positive.	Negative.
Acne	1	0	1
Blastomycosis	3	0	3
Brain tumor	2	0	2
Adenoma	1	0	1
Eczema	1	0	1
Tabes	13	7	6
General paresis	1	1	0
Granuloma	1	0	1
Dermatitis	3	0	3
Chorioiditis	1	0	1
Cancer	3	0	3
Scleroderma	1	0	1
Chancroid	6	0	6
Keratosis palmaris	1	0	1
Salpingitis	1	0	1
Urethritis	1	0	1
Lichen planus atrophicus	1	0	1
Morphea	1	0	1
Morphea guttata	1	0	1
Hepatic cirrhoris	1	0	1
Lymphatic leukemia	1	0	1
Cellulitis	1	0	1
Psoriasis	2	0	2
Papilloma	1	0	1
Pruritis hiemalis	1	0	1
Osteomyelitis	1	0	1
Periostitis	1	0	1
Tuberculous arthritis	2	0	2
Sarcoma	1	0	1
Leucoplakia	3	0	3
Dermatitis exfoliativa	1	0	1
Pityriasis rubra pilaris	1	0	1
Normal sera	13	0	13
Syphilis (hypochondriacal)	30	0	30

TABLE 3.—SYPHILIS †

Case No.	Duration of Infection.	Type of Lesion.	Treatment.		Result of Test.
			Remote.	Recent.	
1	2 years	Late	None	None	+++
6	1½ years	Late	None	None	+++
8	1 month	Early	None	None	+++
9	1 year	Late	None	None	++
10	8 months	Early	None	None	+++
11	5 years	Tabes	1 year	Intermintent	+
12	1½ years	No signs	Continuous	Continuous	—
13	9 months	No signs	Continuous	Continuous	+
14	3½ years	No signs	3 years, Intermittent.	Continuous	—
15	6 weeks	Early	None	None	+++
17	3 years	No signs	Continuous	Continuous	—
20	11 months	No signs	Continuous	Continuous	—
22	15 months	Late	Continuous	Continuous	—
24	4 months	Early	Continuous	Continuous	—
28	2 months	Early	None	None	+++
29	3½ years	Late	2 years	None	—
30	11 months	No signs	Continuous	Continuous	—
31	4 years	No signs	2 years	Few months	+
32	2 years	No signs	Continuous	Continuous	—
36	8 years	No signs	Unknown	None	+
37	2 years	Late	Continuous	Continuous	—
39	7 years	Late	Unknown	6 months	+
41	6 weeks	Early	None	None	—

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TABLE 3.—(Continued)

Case No.	Duration of Infection.	Type of Lesion.	Treatment.		Result of Test.
			Remote.	Recent.	
44	5 years	No signs	3 years	None	—
45	2 weeks	Early		None	++
52	18 years	Late	Unknown	6 months	+
58	1½ years	No signs	Continuous	Continuous	—
60	1½ years	No signs	Continuous	Continuous	+
61	2 years	Late		2 years	—
62	6 weeks	Early	None	None	+++
63	2 years	Late		2 years	+
67	2½ years	No signs		2½ years	—
68	22 years	Late	Unknown	None	+
69	3½ years	No signs	Continuous	Continuous	+++
70	2 months	Early (ch.)	None	None	—
72	8 months	Early	3 months	None	+
73	8 years	No signs	3 years	None	—
76	1 year	No signs	Continuous	Continuous	—
77	16 years	No signs	1½ years	None	—
78	Not K.	Late	Unknown	1½ years	+
79	6½ years	No signs	Intermittent	Intermittent	—
82	15 months	No signs	Continuous	Continuous	+
83	15 years	Late	3 years	None	+
84	5 months	Early		Continuous	+
85	15 months	Early		Continuous	—
86	9 years	Tabes	2 years	Intermittent	—
87	6 years	No signs	3 years	Intermittent	+
88	7 weeks	Early	None	None	+++
89	3 months	Early	None	None	+++
91	2½ years	No signs	2 years	None	—
93	8 years	No signs	2 years	None	+
94	12 years	No signs	Not known	2 years	+
95	4 years	No signs	2 years	Intermittent	—
96	4½ years	No signs	2 years	6 months	+
97	2 years, 3 mos.	Late	Continuous	Continuous	++
98	7 years	No signs	3 years	None	—
100	2 years, 5 mos.	No signs	2 years	None	++
102	4½ years	No signs	2 years	None	—
103	13 months	No signs	Continuous	Continuous	+++
104	8 years	No signs	2 years	None	—
105	15 years	No signs	2½ years	None	—
109	3 years	No signs	20 months	None	—
111	1 year, 9 mos.	No signs	Continuous	Continuous	—
112	13 years	No signs	Continuous	Continuous	++
114	7 years	Late	2½ years	None	++
115	3 years, 4 mos.	No signs	3 years	None	+
116	7 years	Late	2 years	None	+
117	9 years	Tabes	2 years	None	++
118	3 years, 9 mos.	No signs		3 years	++
121	15 months	No signs	Continuous	Continuous	—
123	8 years	Late	3 years	None	—
125	1 year, 8 mos.	No signs	Continuous	Continuous	—
126	4 years	No signs	2 years	None	—
128	2½ years	No signs	Continuous	Continuous	++
129	6 months	Early	Continuous	Continuous	+++
132	5 years	Late	Continuous	Continuous	+
133	15 months	No signs	Continuous	Continuous	+
134	20 years	No signs	Intermittent	None	—
135	Denied	Alop	Not known	None	+++
136	15 years	Headache	Much	Much	+++
137	2 years	No signs	Continuous	Continuous	+++
138	9 years	Tabes	2 years, intermit.	None	+
139	3 years	No signs	2 years	None	++
141	8 years	No signs	Much	None	—
142	6 weeks	Early	None	None	+++
145	2 years	No signs	Continuous	Continuous	—
147	18 years	No signs	2 years	None	+++
148	14 years	No signs	4 years	None	—
149	2 years	Late	Not known	None	+++
150	8 years	No signs	About 3 years	None	+
151	25 years	Tabes	Much	300 gr. K.I. daily	—

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TABLE 3.—(Continued)

Case No.	Duration of Infection.	Type of Lesion.	Treatment.		Result of Test.
			Remote.	Recent.	
153	10 years.....	Late.....	2 years.....	None.....	—
154	3½ years.....	Late.....	3 years.....	None.....	—
158	6 weeks.....	Early.....	None.....	None.....	+++
159	2 months.....	Early.....	None.....	None.....	++
160	15 months.....	Early.....	1 year.....	1 year.....	+++
161	Not known....	Early.....	None.....	None.....	++
163	5 years.....	No signs..	1½ years.....	None.....	+++
164	38 years.....	No signs...	Not known.....	None.....	+
166	15 years.....	No signs...	Considerable.....	None.....	—
168	1½ years.....	No signs..	None.....	15 months.....	+
169	Congenital....	Early.....	None.....	None.....	+++
173	20 years.....	Headache..	Not known.....	None.....	+
174	3 years.....	No signs..	1½ years.....	None.....	+
175	9 years.....	No signs...	Almost continuous.	Almost continuous.	—
176	2 years.....	Late.....	Almost continuous.	Almost continuous.	+
177	2 years.....	Late.....	.....	2 years.....	+
180	20 years.....	Late.....	Not known.....	None.....	—
181	4 weeks.....	Early.....	None.....	None.....	++
182	5 years.....	No signs...	2 years.....	None.....	—
183	1½ years.....	No signs...	Continuous.....	Continuous.....	—
185	2 years, 3 mos.	No signs...	Almost continuous.	Almost continuous.	—
188	3 years.....	No signs...	Continuous.....	Continuous.....	+
189	10 months.....	Early.....	.....	Few months.....	++
190	5 years.....	No signs...	2 years.....	Intermittent.....	—
192	8 years.....	No signs...	3 years.....	None.....	—
193	1 year.....	No signs...	Continuous.....	Continuous.....	—
194	5½ years.....	Generalized alopecia.	2½ years.....	None.....	+
195	9 years.....	Late.....	2 years.....	Intermittent.....	+
196	17 years.....	No signs...	Not known.....	None.....	+
198	5 months.....	Early.....	.....	Continuous.....	+
200	5 months.....	Early.....	None.....	None.....	++
201	1 year.....	No signs...	.....	1 year.....	—
202	2½ years.....	No signs...	Continuous.....	Continuous.....	—
203	6 years.....	Late.....	Not known.....	None.....	—
205	3 weeks.....	Early.....	None.....	None.....	++
207	2 years.....	No signs...	Continuous.....	Continuous.....	—
210	Not known....	No signs...	Not known.....	2 years.....	+
213	9 months.....	No signs...	Continuous.....	Continuous.....	+
214	5 years.....	Late.....	2 years.....	None.....	+
215	2½ years.....	No signs...	Continuous.....	Continuous.....	—
220	1 month.....	Early.....	None.....	None.....	+++
221	8 years.....	Late.....	Almost continuous.	Almost continuous.	+
222	3 years.....	No signs...	2 years.....	None.....	—
223	1½ years.....	No signs...	Continuous.....	Continuous.....	+
224	3 years.....	No signs...	2 years.....	None.....	—
225	7½ years.....	No signs...	2 years.....	Intermittent.....	+
226	14 years.....	No signs...	2 years.....	None.....	—
227	8 years.....	No signs...	About 2 years....	None.....	—
229	6 months.....	No signs...	.....	Continuous.....	++
230	7 years.....	Late.....	2 years.....	Intermittent.....	+
234	12 years.....	No signs...	Moderate amount	None.....	—
236	3 years.....	No signs...	2 years.....	None.....	—
237	10 years.....	No signs...	2 years.....	None.....	—
238	1 year, 9 mos.	No signs...	Continuous.....	Continuous.....	—
240	3 months.....	Early.....	.....	2 months.....	+
241	20 years.....	Late.....	Much.....	Intermittent.....	++
242	15 years.....	No signs...	2 years.....	None.....	—
244	9 years.....	Late.....	About 2 years....	None.....	+
245	9 months.....	Early.....	.....	Few months.....	+
250	15 months.....	No signs...	Continuous.....	Continuous.....	—
251	3 months.....	Early.....	None.....	None.....	+++
252	12 years.....	No signs...	2 years.....	None.....	—
254	15 months.....	Late.....	Continuous.....	Continuous.....	+

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TABLE 3.—(Continued)

Case No.	Duration of Infection.	Type of Lesion.	Treatment.		Result of Test.
			Remote.	Recent.	
258	5 weeks	Early	None	None	+++
259	15 months	Late	Continuous	Continuous	+
262	1½ years	Late	Almost continuous.	Almost continuous.	+
263	1 year	No signs	Continuous	Continuous	+
264	8 years	No signs	About 2 years	None	—
271	6 weeks	Early	None	None	+++
279	1½ years	No signs	Almost continuous.	Almost continuous.	—
280	23 years	No signs	Not known	Intermittent, 14 years.	+
282	8 years	No signs	1½ years	Intermittent	+
283	22 years	Late	Not known	9 months	—
285	3 years	No signs	About 2 years	None	—
289	3 years	Late	Continuous	Continuous	—
291	9½ years	Late	About 2 years	Intermittent	+
293	14 years	Late	Much	Much	+
294	1½ years	No signs	Continuous	Continuous	—
295	9 years	No signs	3 years	None	—
299	1½ years	No signs	Continuous	None for 6 weeks	—
301	1 year, 9 mos.	Late	Continuous	Continuous	+
302	3 years	No signs	Almost continuous.	Almost continuous.	+
303	1 year	No signs	Continuous	Continuous	+
305	4 years	No signs	Not known	Little	++
306	3 weeks	Early	None	None	—
310	3½ years	No signs	2 years	None	—
314	9 months	No signs		8 months	+
320	1½ years	Early	Continuous	Continuous	—
323	2 months	No signs		2 months	—
324	15 years	Late	Several years	None	+
327	6 weeks	Early	None	None	++
331	6 months	Early	None	None	++
332	2 years	No signs	Continuous	Continuous	—
334	20 years	Late	Not known	None	+
335	3 months	Early	None	None	+++
336	4 months	Early	None	None	++
339	1 year, 9 mos.	No signs	Continuous	Continuous	—
340	17 years	Late	Much	Much	+
351	11 years	No signs	About 3 years	None	+
358	18 years	Headache	2 years	None	+
354	5 weeks	Early	None	None	+++
356	8 years	No signs	3 years	None	—
362	2½ years	No signs	2 years, 3 months	None	+
363	5 years	No signs	3½ years	6 months	—
364	12 years	Late	3 years	Intermittent	+
365	3½ years	No signs	2 years	None	—
366	17 years	Late	Much	Intermittent	+
373	2 years	No signs	1½ years	None	—
374	4 years	Late	3 years	None	+
385	9 years	Late	About 2 years	None	+
393	2 months	Early		1 month	+
397	6 weeks	Early		None	+++
400	2 years	No signs	Continuous	Continuous	+
401	8 years	Tabes	2 years	Intermittent	+
404	10 years	Late	3 years	Intermittent	+++
406	12 years	No signs	2 years	None	—
407	6 years	No signs	Almost continuous.	Almost continuous.	+
415	8 years	Late	Almost continuous.	Almost continuous.	+++
417	15 years	No signs	2 years	None	+

†. In this and following table — indicates a negative reaction; +, mildly positive; ++, strong; +++, very strong.

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In Table 4 there are eighty-three cases in which the duration of infection was from one month to three years, the patients having been treated continuously or irregularly for the same period of time. Of this number, twenty-six had manifest signs of the disease, 77 per cent. being positive and 23 per cent. negative. Fifty-seven patients had no signs of syphilis, 42 per cent. of tests being positive and 58 per cent. negative.

TABLE 4.—TREATED CONTINUOUSLY OR IRREGULARLY FROM THE TIME OF INFECTION

Duration of Infection.	Manifest Signs.					No Signs.					Total
	1-6 Mos.	6 Mos.-1 Year.	1-1½ Yrs.	1½-2 Yrs.	2-3 Yrs.	1-6 Mos.	6 Mos.-1 Year.	1-1½ Yrs.	1½-2 Yrs.	2-3 Yrs.	
—.....	1	..	2	..	3	2	4	11	12	13	48
+.....	4	3	4	2	1	..	1	4	2	3	24
++.....	..	2	..	..	1	..	..	1	..	2	6
+++.....	1	..	1	..	1	..	..	1	1	..	5
Total.....	6	5	7	2	6	2	5	17	15	18	83

Manifest signs: Positive, 77 per cent.; negative, 23 per cent.
No signs: Positive, 26% per cent.; negative, 73% per cent.
Total: Positive, 42 per cent.; negative, 58 per cent.

In fifteen cases of the above number giving a negative result, treatment was continued till the day of the test. Later when mercury was discontinued for three or four weeks, a positive reaction was secured in those cases where a second test was made. So it is evident that mercury influences the result of the test in a great many cases. In order to eliminate this factor, treatment should be dispensed with for at least one month before the specimen of blood is taken for examination.

It is interesting to note that some cases of syphilis under vigorous mercurial treatment, regardless of the manner in which the metal is administered, will give a strongly positive reaction even when the treatment is continued till the day of the test; others will become negative with but little treatment. So the question of the virulency of the infection becomes a very important one. This not only depends on the activity of the infecting organism itself, but is also influenced by the

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resistance on the part of the individual. In all probability a patient under treatment, giving a positive test requires a longer period of treatment to effect a cure than one giving a negative result under similar conditions. In the former case, the patient may not be reacting well to treatment or the virulency of the infection may be greater.

TABLE 5.—TWO YEARS OR LESS TREATMENT. DURATION OF INFECTION 3-30 YEARS

Duration of Infection.	Manifest Signs.				No Signs.				
	3-5 Yrs.	5-10 Yrs.	10-15 Yrs.	15-30 Yrs.	3-5 Yrs.	5-10 Yrs.	10-15 Yrs.	15-30 Yrs.	Total
—.....	..	2	1	2	7	10	6	3	31
+.....	1	14	1	4	4	7	2	1	34
++.....	..	1	..	..	2	..	1	..	4
+++.....	1	..	..	..	..	1	..	1	3
Total.....	2	17	2	6	13	18	9	5	72

Manifest signs: Positive, 81½ per cent.; negative, 18½ per cent.
No signs: Positive, 42 per cent.; negative, 58 per cent.
Total: Positive, 57 per cent.; negative, 43 per cent.

Table 5 represents seventy-two cases of patients having had two years or less of remote treatment, the duration of the infection being from three to thirty years. Forty-five of this number were free from signs of syphilis, 58 per cent. being negative and 42 per cent. positive. The remaining twenty-seven cases had signs of the disease, 18½ per cent. being negative and 81½ per cent. positive.

TABLE 6.—TWO TO THREE YEARS' REMOTE TREATMENT. DURATION OF INFECTION 3-20 YEARS

Duration of Infection.	Manifest Signs.			No Signs.			Total.
	3-5 Years.	5-10 Years.	10-20 Years.	3-5 Years.	5-10 Years.	10-20 Years.	
—.....	1	1	..	4	7	1	14
+.....	..	..	3	2	1	2	8
++.....	..	..	..	..	..	..	..
+++.....	..	..	1	1	..	..	2
Total.....	1	1	4	7	8	3	24

Manifest signs: Positive, 66⅔ per cent.; negative, 33⅓ per cent.
No signs: Positive, 33⅓ per cent.; negative, 66⅔ per cent.
Total: Positive, 58⅓ per cent.; negative, 41⅔ per cent.

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In Table 6, there are twenty-four cases of three to twenty years duration, and from two to three years remote treatment. Of these 58⅓ per cent. were negative and 41⅔ per cent. positive.

TABLE 7.—TREATMENT NOT KNOWN. DURATION OF INFECTION 3-30 YEARS

Duration of Infection.	Manifest Signs.					No Signs.					Total.
	3-5 Yrs.	5-10 Yrs.	10-15 Yrs.	15-20 Yrs.	20-30 Yrs.	3-5 Yrs.	5-10 Yrs.	10-15 Yrs.	15-20 Yrs.	20-30 Yrs.	
—.....	..	4	..	..	2	..	3	9	4	3	25
+.....	..	5	2	7	..	..	..	2	1	1	18
++.....	..	..	2	..	1	1	..	2	..	..	6
+++.....	..	1	1	..	..	..	..	..	..	..	2
Total.....	..	10	5	7	3	1	3	13	5	4	51

Manifest signs: Positive, 76 per cent.; negative, 24 per cent.
No signs: Positive, 27 per cent.; negative, 73 per cent.
Total: Positive, 51 per cent.; negative, 49 per cent.

Table 7 represents fifty-one cases in which the duration of infection was from three to thirty years, the amount of treatment being unknown. In twenty-five of this number, signs of the disease being present, 76 per cent. were positive and 24 per cent. negative. Of the remaining twenty-six cases without signs, 27 per cent. were positive and 73 per cent. negative.

TABLE 8.—TREATMENT AND DURATION OF INFECTION UNKNOWN

	Manifest Signs.		No Signs.	Total.
	Early.	Late.		
—.....	..	4	9	13
+.....	1	19	2	22
++.....	2	10	1	13
+++.....	..	12	..	12
Total.....	3	45	12	60

Manifest signs: Positive, 91⅔ per cent.; negative, 8⅓ per cent.
No signs: Positive, 25 per cent.; negative, 75 per cent.
Total: Positive, 78⅓ per cent.; negative, 21⅔ per cent.

In Table 8, there are sixty cases in which the duration of the infection and amount of treatment are not known. Forty-eight of these had manifest signs 91⅔ per cent. being positive and 8⅓ per cent. negative. The remain-

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ing twelve patients were without symptoms of syphilis; 75 per cent. were negative and 25 per cent. positive.

In Table 9, thirty-six patients with manifest signs and no treatment gave 86 per cent. positive and 14 per cent. negative reactions. Four of the five negative cases were in the chancre stage of the disease.

TABLE 9.—NOT TREATED

Duration of Infection.	Manifest Signs.				Total.
	1-6 Months.	6 Mos.-1 Yr.	1-2 Years.	2-5 Years.	
−.....	5	..	..	..	5
+.....	2	..	..	..	2
++.....	7	1	..	..	8
+++.....	17	1	3	..	21
Total.....	31	2	3	..	36

Positive, 86 per cent.; negative, 14 per cent.
Note.—In four of the five negative cases the exanthem had not appeared.

From a study of these cases we can readily see that in a large percentage of cases two or three years of treatment even when continuous is not sufficient to eradicate the disease. The patient may have had no signs of his trouble for many years and believe himself entirely cured, yet when the test is made, evidence of the old infection are shown when a positive reaction is secured.

In latent syphilis where the patient has been free from symptoms for a number of years and the disease again makes its presence known by signs or symptoms referable to the skin, the central nervous system, or some one of the viscera, the question at once arises, where has the hidden and concealed focus been located? There seems to be no doubt that such a focus of infection may be present in a great many cases, and, being walled off by connective tissue in Nature's attempt to overcome the disease, may lie dormant for variable periods of time, until, owing to some unknown etiological factor, the spirochetes and their toxins are taken up by the blood and lymph and carried to all parts of the body. A positive serum test in such cases would be expected even if at some former date it had been

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negative, owing to the quiescent state of the concealed focus of infection. When these walled-off foci are on the surface of the body, it is not difficult to secure a few drops of serum from the lesion to be used in the test; at the same time serum from the patient's blood can be tested and the difference in strength of reaction noted. In Case 228 of this series, the serum from the blood was negative, while the serum from the lesion on the patient's arm, which had been present five years, gave a strongly positive reaction. In Case 404, both the serum from the blood and that from the lesion were strongly positive. More work along this line will be necessary before final conclusions can be drawn; but we are led to believe that in such cases a protecting wall of tissue is preventing the organism and their toxins from entering the general circulation in any appreciable amount. This condition would explain why we get so many negative reactions in cases where there are evidences of the disease, and positive results where no signs of syphilis can be found; the focus being concealed in some part of the body not accessible to touch or vision. If such a condition is possible, the difficulty in clearing up some of the latent lesions which do not react readily to vigorous specific treatment is more readily understood, as but little if any of the medicinal preparation penetrates the protecting wall of tissue. The palmar and plantar syphilides are striking examples of this class of cases.

CONCLUSIONS

1. In serum diagnosis of syphilis a positive result is an indication that the disease is still active and that more treatment is necessary.

2. One negative result should not suffice in any suspected case of syphilis. The test should be repeated at intervals of six months for the first year after all treatment is discontinued and afterward at longer periods.

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3. In quite a large percentage of cases two years of specific treatment, regardless of the manner in which it is administered, is not sufficient to insure a negative result from the serum test.

4. The tendency at the present time is rather to give insufficient treatment in syphilis than to over-treat the disease.

5. The Wasserman test is of inestimable value in obscure cases of syphilis, and in differential diagnosis.

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TWO YEARS' EXPERIENCE WITH THE WASSERMANN REACTION IN PRACTICE

A PRELIMINARY REPORT ON FIFTY-SEVEN CASES TREATED FROM THE STANDPOINT OF THE WASSERMANN REACTION

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The years 1903, 1905 and 1907 each marks a definite step in the advancement of our knowledge of syphilis.

With Metschnikoff's and Roux's inoculation experiments on the higher apes in 1903 the scientific world again renewed its efforts to discover, if possible, the cause of syphilis, and when Schaudinn and Hoffmann announced the *Spirochæta pallida,* in 1905, the diagnosis of primary syphilitic lesions was placed on a definite basis.

The establishing of the *Spirochæta pallida* as the etiologic factor in syphilis has been fraught with much criticism, because the discovery did not conform to Koch's postulates. The work of Metschnikoff, Roux, Neisser and many others stands out in bold relief and has put the specificity of the *Spirochæta pallida* on so firm a basis that, notwithstanding their inability to culture the organism, it is now accepted by syphilographers the world over.

The complement-fixation test as discovered by Bordet and Gengou, and elaborated by Wassermann, Neisser

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and Bruck, has brought us in still closer relation with this universal disease. Like the *Spirochæta pallida,* it has had its full share of criticism and condemnation, a large part of which was due to imperfect technic and application. That it is absolutely specific and of immense clinical value is a conclusion that can be drawn from the many reports that have appeared in the literature and the thousands of cases that have been examined.

The Wassermann reaction is valuable for both the general practitioner and the specialist. Neisser[1] says that the Wassermann reaction reveals syphilis with such certainty that nothing would induce him to dispense with it now.

Positive findings are a distinct indication of existing syphilis, and repeated negative findings are extremely valuable for a favorable prognosis, although the test is not infallible in every case. It is as important for the general practitioner as is the microscope for the determination of gonorrheal secretions. The Wassermann test is most valuable for the syphilographer, not only as an aid in the diagnosis but also in the treatment of syphilis. Until the discovery of the *Spirochæta pallida* and the application of the Wassermann test little indeed was known about this universal disease, save what could be seen externally and on the mucous surfaces. With the introduction of these two means of diagnosis we have at last something tangible to work with. It is possible now to make an exact diagnosis and to begin treatment at once, telling the patient with some degree of assurance what his future may be.

Höne[2] analyzes the findings in 1,512 cases of certain and of suspected syphilis and in 320 non-syphilitic patients. The findings confirm the specific importance of the test and show that energetic mercurial treatment

1. München. med. Wchnschr., May 25, 1909, lvi, 1057.
2. Berl. klin. Wchnschr., May 10, 1909, xlvi, 862.

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is able to transform a positive into a negative reaction in a large proportion of cases.

A positive reaction was obtained in 23 out of 107 prostitutes with apparently no signs or history of syphilis.

Boas[3] has applied the Wassermann test in 1,345 cases. He states that positive findings after systematic treatment of syphilis are invariably the precursors of a recurrence. The serum test applied once a month in the first years after infection, and the resumption of treatment in case of positive findings, will certainly have a marked influence in warding off recurring trouble.

Purkhauer[4] reports from Neisser's clinic the findings of the Wassermann test as applied to 5,200 cases of syphilis. The findings were positive in inverse proportion to the number of intermittent courses of treatment that had been applied in the individual cases. The more energetic the treatment, the smaller the proportion of positive reactions. A single course of treatment does not seem to have much effect on the outcome of the test, but the general impression is all in favor of a thorough treatment in the first months and years after the infection.

W. Scholtz[5] says that the Wassermann reaction is generally negative from the third to the sixth week after infection, and as a consequence it is only of slight value for early diagnosis.

Therapeutically the Wassermann test is of importance because it indicates that it is possible in a degree to cure syphilis by abortion, but the proof cannot be substantiated without further observation, extending over years.

Jesionek and Meirowsky[6] say that we should bend every effort to change a positive to a negative reaction, because every syphilitic with a positive reaction is in danger of tabes and paralysis.

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3. Berl. klin Wchnschr., March 29, 1909, xlvi, 577.
4. München. med. Wchnschr., April 6, 1909, lvi, 697.
5. Deutsch. med. Wchnschr., February, 1910, No. 5, p. 215.
6. München. med. Wchnschr., 1909, lvi, 2291.

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The earlier the treatment commences and the more energetically it is carried out the sooner will a positive reaction become negative. Chronic intermittent treatment unquestionably gives the best results, but we cannot as yet say whether this can make a negative reaction permanent.

It is true that these discoveries may dull the diagnostic shrewdness of the clinician and in time lessen his ability, but, like all biologic tests, they should be used as adjuncts, not as first aids, in diagnosis.

I have been working two years with the Wassermann reaction in practice. I began with the original Wassermann technic and have adhered to it throughout the whole time.

In reporting these cases, care has been taken to note carefully the results in making the Wassermann test. Alcoholic extract of a liver of a congenital syphilitic was used as an antigen, with plenty of known normal and syphilitic serums as controls, and each tube was tested twice with different strength antigens, each acting as a control for the other.

For convenience I have adopted the following classification:

Group I. New cases treated after the biologic method.
- A. Chancre, *before* the Wassermann reaction was positive.
- B. Early secondaries, *after* the Wassermann was positive.

Group II. Old cases treated before the biologic method was used.
- A. Late secondaries.
- B. Latent.
- C. Tertiary.
- D. Congenital.

Group III. Apparently cured.

GROUP I: A. CHANCRE BEFORE WASSERMANN REACTION WAS POSITIVE

All patients presenting themselves for examination were treated in the following routine manner: Diligent search was made in the primary lesion for the *Spiro-*

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chæta pallida. If this was not successful, puncture of the inguinal glands was resorted to and, regardless of whether the diagnosis was conclusive or not, a Wassermann test was made. This gave me immediate control of the diagnosis. I found that the Wassermann reaction was positive in direct proportion to the time of the presence of the primary lesion.

Depending on the length of time of the presence of the primary lesion, excision of the chancre was practiced whenever it was possible; however, rarely later than the tenth day or second week, as later than this systemic involvement to some degree has, as a rule, taken place.

In this series there were seven cases. In five of them excision was employed; one was situated in the coronary sulcus beneath the frenulum and could not be removed without great destruction of tissue; one was treated locally with calomel.

I still warmly advocate the principle of excision, but believe it to be a dangerous procedure for the operator, as a needle-prick or an excoriation on the finger may easily become the atrium of infection.

In examining many lesions that had previously had calomel used as a dusting powder, invariably the spirochete was not to be found, or if found at all it was with difficulty, showing that mercury in this form has some action locally in the destruction of the spirochete. I offer this time-worn method as the best both for the patient and the surgeon. Some may argue that this does not accomplish the desired effect; i. e., the removal *en masse* of the first known collection of spirochetes. This cannot be proved unless sectional stains are made. It seems perfectly rational to assume that if calomel has such a marked local effect on the spirochetes as to prevent their being found in the serum of the initial lesion, its free use should act as an efficient substitute for the highly scientific but hazardous procedure of excision.

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Whenever it was possible to make a diagnosis from the primary lesion, the blood for the Wassermann test being previously taken, an injection of mercury was given at once, the object being to begin treatment at the earliest possible moment after a positive diagnosis was made, with the sole idea that if the blood test showed negative it should be kept so; if it showed positive it should be made negative and kept negative throughout the whole time.

Of the seven patients, the first two discontinued treatment after three months, but up to this time neither had even an adenopathy. Both have disappeared. Of the other five, one relapsed, and at the time of his second blood test, which was positive, he had plaques on his tonsils. The remaining four have continued along in an even, uninterrupted course. Wassermann examinations were made at intervals, on an average, of from four to six months.

The most recent case was of five months duration, the patient had two blood tests and both were negative.

TREATMENT

In these cases the treatment was most energetic; except for a few injections, rubbings and internal treatment were the regular routine. Where the patient could afford it, I preferred to have a masseur give the rubbings.

Some observers have argued that beginning treatment so early predisposes to the parasyphilids, as these patients are not sufficiently impressed with the severity of their own clinical picture and soon stop treatment. This in a measure is true among a certain class of patients, but it is equally true that patients of this class will do exactly the same thing if permitted to wait for secondaries before beginning treatment; they will treat until symptoms disappear and then stop. I believe that relapses would be fewer and that our success would be greater if vigorous treatment were instituted before

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the body was fairly saturated with the spirochetes, taking it for granted that the patient will only submit to treatment for a short while.

In this series the four cases that have remained with a negative Wassermann reaction have not had the slightest sign of syphilis, and except for the sites of their initial lesions they are absolutely clean.

GROUP I: B. EARLY SECONDARIES AFTER THE WASSERMANN REACTION WAS POSITIVE

In this series there are eleven cases; seven have become negative; four have remained positive. In the seven cases that obtained a negative, one patient relapsed, but has since regained a negative. All the other cases that obtained negatives have continued along without any unfavorable symptoms.

The shortest time in which I was able to change a positive Wassermann reaction in a patient with a papular eruption to a negative was two and one-half months. The patient had rubbings and internal treatment, rubbing an even 300 gm. of mercury in succession.

Of the four patients who did not progress, two absolutely gave up, preferring an easier method of living; two made several attempts at continuous treatment, but were not successful.

GROUP II: A. LATE SECONDARIES

In this series, in which the patients began treatment with external symptoms before the biologic treatment was in use, there are thirteen cases. All have had external manifestations within one year except two cases; the infections date from three to eight years prior to observation. Twelve patients have continued treatment; one has dropped out. Of the twelve that have continued treatment, it has been possible to obtain and continue a negative Wassermann reaction in only two, and these are two that have shown no external manifestations of syphilis for two years.

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Three cases in this group presented spirochetes in the mouth in mucous plaques four, six and eight years after infection. The older the infection with active lesions the more difficult it seems to be to get a negative Wassermann reaction. Some of these patients were on their one hundred and fiftieth rubbing with only short intermissions between treatments.

It is here that one begins to see a direct relationship between a positive Wassermann reaction and persistent infections. All of these patients presented themselves for treatment from the eighteenth month to the fourth year after infection, and in one instance eight years. Their treatment from the beginning had been of a mild, intermittent, chronic type, so that at the time of beginning treatment under the biologic method they were, so to speak, thoroughly impregnated with the spirochetes.

GROUP II: B. LATENT CASES

In this series there are fifteen cases. All gave a typical syphilitic history but were free from external signs of syphilis for three years, and longer in some instances. All showed a positive Wassermann reaction.

Seven of these cases obtained a negative Wassermann reaction; of the seven, four relapsed. Of the eight remaining cases one discontinued treatment; the remaining seven were not able to obtain a negative blood test.

GROUP II: C. TERTIARY

In this series there are two cases.

CASE 1.—Infection eighteen years ago; one and one-half years ago gumma of finger. Wassermann reaction positive. In spite of fairly vigorous treatment this case had remained unchanged at the last examination three months ago.

CASE 2.—Infection nine years ago; three years ago gumma of left testicle, which promptly disappeared under specific medication; treatment vigorous at the onset, but later desultory, and still later discontinued. Blood-test always positive.

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The discouraging results in Group II, B and C are attributed to the following circumstances:

1. Latency of infection: apparent freedom from the disease, so far as symptoms go.
2. Inability to apply continuous energetic treatment for any length of time.
3. Energy and financial resources exhausted in long continued treatment.
4. The difficulty of convincing the layman of the significance of a positive Wassermann reaction in the face of apparent good health.

GROUP C.—APPARENTLY CURED*

Patient.	Time of Infection, Years Ago.	Kind of Treatment.	Last Treatment, Years Ago.	Biologic Test.
G. K.....	12	Internal and rubbings, fairly vigorous.	4	Test 1 neg., 8/ 1/08
C. K.....	6	Internal, injection, rubbings, chronic intermittent form.	2	Test 1 neg., 4/ 1/09 Test 2 neg., 11/ 1/09
A. C.....	5	Internal, rubbings and injections, vigorous.	1½	Test 1 neg., 7/ 5/09 Test 2 neg., 3/ 1/10
L. D.....	12	Rubbings, internal and injections.	3	Test 1 neg., 2/ 1/09 Test 2 neg., 8/ 1/09 Test 3 neg., 3/ 1/10
J. M.....	19	Internal, injections and rubbings.	5	Test 1 neg., 5/ 4/09 Test 2 neg., 2/10/10
S. C.....	8	Injection, rubbings, internal, chronic, intermittent form.	1½	Test 1 neg., 6/ 1/09 Test 2 neg., 2/ 2/10
R. C.....	5	Rubbings, injections and internal, vigorous.	1½	Test 1 neg., 8/ 2/09

* In this series there are the seven cases here given.

GROUP II: D. CONGENITAL SYPHILIS

In this series there are two cases.

CASE 3.—Male child, son of a male patient of mine who was married in the second year after his infection. Patient was under observation for five years. Treatment was begun in the second year, at which time there was only anemia and general adenopathy, with slightly stunted growth.

Blood-test was positive two years ago; one year later negative, and in April, 1910, negative again, with no treatments in the interim.

CASE 4.—Male; came under observation in the ninth year, after his infection, with many typical signs of congenital syphilis: had had many courses of mercury. Eighteen months ago blood-test was positive. Almost continuous treatment for

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the following eighteen months gave no success so far as a negative blood test is concerned, three examinations being made.

This boy is in apparently good health and is able to work as a messenger, having graduated from the grammar school last spring. As suggested by Purkhauer[6] and Bruck,[7] it is a question whether this case can ever become negative.

In this series the more favorable cases are the older ones with a corresponding repeated negative biologic test. Those of more recent origin, with vigorous treatment and two or more negative biologic tests, I regard as likewise favorable; whether they will relapse again time alone will tell. To guard against any further trouble it will be necessary to make a Wassermann test from time to time in such a manner that the test will become necessary less often the further back the primary infection lies, provided that the reaction has been found negative on several tests repeated from year to year.

If this so-called biologic method is to be adopted it will be necessary for us to lay new foundations in the way of treatment. If we expect to maintain a negative Wassermann in a given patient the treatment must be continued after the negative goal is reached, as withdrawing treatment at this time only permits of the rehabitation of the patient by the spirochetes, with a resulting positive biologic test.

How long this vigorous treatment is to be continued the future will have to decide. It may be possible to prophesy one and one-half to two years, but the test is far too recent to permit any definite conclusions. It is true that some of these cases may develop a Wassermann-ophobia, but beyond this, with careful examination of the urine and gums and attention to general hygiene, these patients should show only steady improvement.

CONCLUSIONS

The biologic treatment of syphilis seems to offer a tangible guide in the management of syphilitic cases.

7. Bruck: Die Serodiagnosis der Syphilis, Berlin, 1909.

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For its successful culmination it is positively necessary to have:

1. An early diagnosis, either by finding the spirochetes in the lesions, or by the positive serum reaction of Wassermann.

2. Control of the treatment by biologic tests; not by the clinical manifestations of the disease.

100 State Street.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. WAUGH AND COBBUS

DR. J. GRINDON, St. Louis: There is probably not a man in the room but could relate a number of striking instances bearing on the Wassermann test. I will limit myself to one. Six years ago, a young attorney came to me with the history of an initial lesion, which was followed by a papular, secondary eruption. He was at once put under active treatment, and remained under such treatment and observation for three years, developing no further symptoms. At the end of that time he was apparently in splendid health. At intervals of three or four months he would come in and see me, when I would tell him that to the best of my knowledge he was well. A year ago last June I explained the Wassermann test to him, and advised him to submit to it. He did so, and the reaction was positive. He returned home and submitted to a mercurial course, which, contrary to my advice, was taken internally instead of by injection. Six months later, which was five and a half years after his last symptom, he wrote to me that a painful growth was developing above the inner condyle of the humerus. I examined him carefully, and in spite of what I knew of his history, believed that the growth was probably a sarcoma. We cut down on it and found a gumma. The case presents a striking confirmation of the value of the Wassermann test.

DR. M. L. HEIDINGSFELD, Cincinnati: There is one phase of the Wassermann test to which I wish to direct special attention. Cases of syphilis, after treatment has been instituted, frequently develop a negative Wassermann, sometimes after very little treatment. On the other hand, other cases, in spite of very vigorous treatment, will show a decidedly positive reaction for a long period. This is probably due to the fact that the Wassermann test is a test of "antibodies," or the reaction of the system against syphilis, and not of the virus itself. In two cases of malignant syphilis on my service at the Cincinnati Hospital, in which both patients developed early rupia, and the malignant nature of the disease was well defined in all its aspects, the Wassermann reaction was negative from the very

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beginning, and in spite of the most energetic mercurial and arsenical treatment, it never gave a single positive reaction after repeated tests. One of the patients died eighteen months after infection; the other is still alive, but is in desperate straits. These patients have never reacted against the disease; probably no antibodies were formed, and the Wassermann test was therefore negative.

DR. J. A. FORDYCE, New York: I have watched the results of the Wassermann reaction during the past two years in my private and public practice, and these observations have led me to the belief that it is a method of great diagnostic importance. Regarding its practical or therapeutic application, it seems to emphasize the fact that mercury given hypodermically or by inunction has a greater influence over the reaction than mercury given internally. Furthermore, the earlier the treatment of the disease is begun the sooner the reaction becomes negative. It may be stated conservatively, I think, that the treatment of syphilis as generally carried out is very inefficient; that mercury is given in too small doses and that the use of potassium iodid is only exceptionally indicated in the secondary stage of the disease, though frequently it is relied on by practitioners from the beginning.

DR. WILLIAM LITTERER, Nashville, Tenn.: I have made Wassermann tests, using different antigens, in twenty cases of pellagra. Three out of the twenty reacted positively. In one out of the three positive cases there was a history of syphilis; in another, an indefinite history of lues. I do not believe that the Wassermann reaction will be positive in non-syphilitic cases of pellagra; and this is in accordance with the experience of Dr. Howard Fox, although Bass has reported positive reactions in practically every case examined by him. In our cases we employed both the original Wassermann and the Noguchi tests, and both gave uniformly negative results.

I have found that in some cases, the use of the protoiodid of mercury internally does not obliterate the Wassermann test, but when we change to the inunction method, it usually becomes negative in a fairly short time. In some cases, the inunction method seems to be more efficacious than the injection method, and *vice versa*. We cannot be absolutely positive which is the better method, but I agree with Dr. Fordyce that either is preferable to the internal method.

DR. WILLIAM T. CORLETT, Cleveland: I think we are generally agreed as to the value of the Wassermann reaction in syphilis. A year ago I spent some weeks in the laboratory of Professor Finkler at Bonn, working up the Wassermann reaction. The difficulties in carrying out the reaction in private practice are great, and I think it should be largely left to men doing laboratory work. This applies not only to the technic, but to the skill and experience necessary to read the reactions aright. There is another point I wish to refer to, and that is

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the influence the Wassermann reaction may have on our therapeutic methods in the treatment of syphilis. For a number of years, my observations have taught me that cases of syphilis treated with any form of iodin during the early stage of the disease run a more protracted course and prove more obstinate to treatment than do cases in which iodin has been withheld. Further, I have long been convinced that mercury is the only drug that has any definite and constant influence in eliminating the syphilitic virus. Both observations have been verified by the Wassermann reaction.

DR. ALFRED SCHALEK, Omaha: I wish to report a case that came under my observation lately. The case was one of syphilis, pursuing a very malignant course, but under persistent treatment with inunctions and injections the symptoms finally cleared up. The patient subsequently went to Europe where he saw Prof. Neisser, who had a Wassermann test made, which proved negative. A similar test was afterward made by Dr. Schamberg of Philadelphia and was again negative. Shortly after that the patient developed symptoms pointing to a syphilitic brain lesion, and he is in a hopeless condition today. Our indications are clear when the Wassermann test is positive, but how do we stand as to the continuation of treatment when it is negative?

DR. E. H. MARTIN, Hot Springs, Ark.: I was very much interested in the statement made by one of the speakers that the spirochetes might remain sealed up in the connective tissue for a number of years, and that under those conditions, mercury was not effective. I was also interested in the statement made by Dr. Corlett that mercury was the only drug that was effective in controlling this disease during its early stages. That I believe is a mistake. We have in the arylarsonates a powerful remedy for the treatment of early syphilis. I have used the various preparations of the arylarsonates in about 200 cases of syphilis, and while I am not prepared to say that with them I am satisfied to get along without mercury in the treatment of this disease, yet I have found them very effective. Under the use of these remedies the lesions cleared up in at least one-third of the time that they would with the iodids, and in one-tenth of the time that they would with mercury alone. Arsenic, we know, has the power to penetrate the tissues, and hence may destroy spirochetes sealed up against mercury. In the case reported by one of the speakers here today, where the Wassermann test gave a negative reaction in the face of marked pernicious syphilis, I can almost promise him that the symptoms in such a case will respond to the arylarsonates.

DR. ALFRED SCHALEK, Omaha: In the case I reported, the symptoms failed to yield to any of the preparations of arsenic.

DR. EDWARD BOWE, Jacksonville, Ill.: I am more particularly interested in this subject from the standpoint of mental and nervous diseases, as I have seen a number of cases of

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teritiary brain lesions. Presuming, as a neurologist, that one is called on to make the differential diagnosis between a specific lesion of the brain and a brain tumor, one can readily appreciate the importance of having such a test as the Wassermann reaction to fall back on. In many such cases we get a very obscure history of syphilis, or none at all. Given a history of syphilis, the treatment may have been inadequate or inefficient, and under such conditions you can readily see the value of such a diagnostic test as this. If the reaction was positive, it would give us a direct indication as to treatment and aid us in the prognosis. The same applies in dealing with obscure cord lesions.

DR. OLIVER S. ORMSBY, Chicago: In our office it has now become a routine measure to examine all doubtful cases of syphilis by the serodiagnosis test. In cases in which syphilis is shown to exist, the treatment should be continued as long as the test is positive. Some authorities say that a patient with syphilis should be treated as long as he lives; others differ from this view. It is evident that in some individuals syphilis persists for many years, while others recover promptly. The results of the Wassermann test confirm this. Some cases show a negative reaction after a few months, while others persist in giving a positive reaction in spite of long-continued treatment: the latter are usually of the virulent type. As an example the following case is cited: A patient developed a profuse exanthem of the florid type; this disappeared under energetic treatment, mercury being given by injection, inunction and internally at different times during two years of constant treatment. Three months after he was discharged his blood was tested and gave a positive Wassermann reaction. At the time the patient was apparently healthy and had exhibited no symptoms of syphilis since the first outbreak two years previously. Before we had time to institute further treatment, he developed paralysis of the third nerve, and since then he has had almost uncontrollable symptoms. The Wassermann test is a most valuable addition as an aid in diagnosis and should always be considered in conjunction with our knowledge of the clinical manifestations of syphilis.

DR. V. J. COHENOUR, Joliet, Ill.: In reply to Dr. Bowe I would say that a patient may have a non-syphilitic brain tumor and still have syphilis, and in such a case the Wassermann reaction would not throw much light on the differential diagnosis. If the case is one of brain syphilis without a brain tumor, the chances are that the symptoms will clear up under anti-syphilitic treatment, whereas in brain tumor you would get at best but a temporary remission of the symptoms. The fact I wish to bring out is that we may have a combination of these two conditions. I have seen individuals with chronic syphilis in whom the Wassermann test gave a negative reaction at one time, and a strongly positive reaction perhaps six

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months later. In some cases of gumma, for instance, where a negative reaction is obtained, the administration of potassium iodid for some time may be followed by a positive Wassermann, indicating that the drug has stirred up some of the syphilitic products. As to the curability of syphilis, I think that when once a man has syphilis, he always has syphilis. I have examined men who were treated in the ordinary way for ten or fifteen years, and thoroughly treated, and still, in spite of that, they showed decided symptoms of the disease later on. I have found that by the inunction method of treatment the reaction is decidedly quicker than by any other. Next to this, I favor the injection method, and lastly, internal treatment. The test I prefer is the unmodified Wassermann, and I do not find it particularly difficult.

DR. J. F. WAUGH, Chicago: My experience with this test in the field of nervous diseases has been rather limited. In the series of cases reported, there were thirteen cases of tabes, seven being positive and six negative; and two cases of general paresis, both positive. In cases of suspected syphilitic involvement of the central nervous system, the test is of the greatest value. However, a negative result does not preclude the possibility of syphilis, as the results of practically all investigators in latent syphilis will prove. Judging from the effect of treatment in converting a positive into a negative result in a given case, it would seem that the most efficient manner of administering mercury is by injection or inunction. Even after a negative result is secured and the patient is apparently free from his disease, the test should be repeated at intervals for a number of years. In this manner it is quite probable that many of the late manifestations of the disease can be prevented. Future work along this line will undoubtedly disclose interesting facts.

DR. B. C. CORBUS, Chicago: In order to get accurate results from these tests we must of course have a good laboratory, and the technic must be faithfully carried out. When the result is positive, it demands early and energetic treatment.

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THE DIAGNOSIS OF LEPROSY

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NEW ORLEANS

Long association with the Louisiana Leper Home has given us an opportunity for the observation of leprosy, and we hope that this, together with the importance of correct and early diagnosis, in countries where leprosy is likely to occur, will justify the present discussion of this subject. We are not submitting any new points in diagnosis but rather argue the need of a practical presentation of the matter for the general profession, especially in our own country, where every now and then a notable case proves an ignorance of essential points which should be known. More than this, the reports of imported cases of leprosy in our seaport cities have shown conclusively either that the national quarantine against leprosy is a farce in its enforcement, or that the quarantine officials are ignorant of the symptoms of the disease. In New York chiefly numerous cases have been presented which have more or less recently been admitted to this country without hindrance.

As a matter of fact, the increasing number of lepers in New York has grown by importation, as the disease so far is not held endemic there.

The trouble in diagnosis lies more with atypical cases, with incipient tubercular cases and with those anesthetic

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cases which present no longer active skin manifestations. Another source of confusion in diagnosis lies in the changes that appear in lesions during the periodic occurrence of exacerbations accompanied by lepra fever.

Like syphilis, leprosy has often been divided into stages and types, but, as in syphilis, the value of such diagrammatic classification of leprosy is greatly impaired by the fact that the types are often mixed and that the lesions that should be present in one stage are often found in another. Generally the type depends on the habitat of the bacillary cause, the anesthetic or trophic being due to nervous injury by the bacilli, the tubercular or nodular being due to the presence of the bacilli in the skin, and the mixed type being a combination of the anesthetic and tubercular forms. It is not unusual in the course of years to see a change in the type. The tubercular type in a mixed case may disappear, leaving only the anesthetic, and a purely anesthetic case may after years develop tubercles, forming the mixed type, which may, in turn evolve a trophic type, having no tubercles in evidence.

The usual sequence of the lesions after the prodromal period is that the first manifestation in almost every case is in macules which usually initiate all types, usually varying in their location accordingly. Much rarer is the bullous eruption which occurs in this same early stage. Tubercles usually appear later than macules and may be independent of them; the ulceration and cicatrization of the skin occur ordinarily only in the terminal stage, though the perforating ulcer, which is a sinus leading to necrotic bone, may be found early, and in mutilating types the erosions following bullous leprosy may form true ulcers before any macules or tubercles present themselves.

The macular eruptions do not always present the same characteristics. They vary from the size of a dollar, or smaller, to a patch large enough to cover an entire anatomic region; the pigment may be almost uni-

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formly distributed throughout the patch, as it is in chloasma, or it may disappear in the center, leaving a ring of pigment surrounding an area of skin lighter in color than the normal; somewhat the same arrangement that ringworm of the general surface assumes, except that the atrophy of pigment in the center is marked and may, at the same time, involve the deeper skin. Scales are unusual in both types and occur usually only as a result of inflammation in the area or as the evidence of trophic disturbances.

The first type, the uniformly pigmented macule, depends largely for its characteristics on the amount of infiltration provoked by the presence of the bacilli. It may be simply a brown stain, level with the surface of the skin, with an irregularly shaped border not always marginated, or a patch so elevated that the term macule becomes a misnomer. On the other hand, there may be multitudinous macules, with symmetrically bilateral distribution on the trunk and extremities alike, entirely free of bacilli and having all the characteristics of a true erythema.

This form of macule is particularly common in anesthetic leprosy in which the early involvement of the nerve trunks of the extremities points to the toxic influence of the leprous deposits along the nerves. This is particularly argued in the facts that such eruptions of macules are evanescent and that the lesions themselves are highly colored, bright red, and are often apt to be hyperesthetic and not anesthetic as are the more deeply pigmented and infiltrated lesions.

In the second form the margin is well defined and the brown color becomes a purplish red. Between these two extremes are the variations in shade made possible by the varying degrees of inflammatory infiltration. The favorite location is the buttocks, though the face, trunk and limbs may also be involved, and these macules are often the sites of later tubercles or nodules, especially when found on the face. Though these may not be

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necessarily symmetrical when they first appear, later these macules become so as the eruption fully develops. During the periods of lepra fever the macules may become intensely inflamed and painful, and though the fever does not usually occur severely during the incipient period, we have had at the Louisiana Leper Home instances in which the whole macular areas, numbering four or five as large as the palm of a child's hand, have ulcerated. Ulceration in the incipient stage is indeed rare, and can be explained only by the lepra fever, which is evidently a manifestation in greater or less degree of fulmination of deposits of lepra organism, or else the acute reaction associated with new fields of invasion.

In the circinate type the patch of lepra macules usually grows in size after it first appears, spreading from the outer border of the ring, which preserves a well-defined margin; and it is more often associated with the anesthetic than the tubercular form. The inner margin of the ring is not liable to show as well-defined a border as the outer, and as the lesion grows larger in area the paler center grows also, keeping the pigmented ring nearly constant in relative breadth. The degree of infiltration in this type of macule is not as variable as in the first type, usually remaining slight, and the color varies with the depth of infiltration. This, too, is found almost always as a light brown, aptly described as *café au lait,* which is the characteristic color of all of the macules that present the least amount of infiltration. A reddish tinge is added to the brown of the border in those cases with more marked infiltration, the resultant color being a red-brown, which is again intensified during the lepra fever. This circinate type may occur on any part of the body, but the hands and head are not as liable to this as to the form in which the macule presents a uniformly pigmented area, appearing *en plaque.* The areas of especial predilection are the shoulders, legs, thighs, buttocks and forearms, in the order named. It is not infrequent to find confluent

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lesions of this type forming grotesque ribbons of irregular borders and outlines, extending alone the whole of an extremity or showing symmetric figures over the back.

The bullous eruption, which is very rarely seen, occurs associated with this early stage, or precedes the macule if it occurs at all. The bullæ contain serum at first, but become pustular in a short time. They are not larger than a small marble, and occur most frequently on the hands and feet. The clinical diagnosis is fre quently difficult without other evidences of the disease. The bullæ have a predilection for the areas over the knuckles of the fingers and will repeatedly appear in the same site, establishing scar areas with encircling pigment, which is characteristic. Often these lesions lead to ulceration and even trophic changes· in many cases misleading to a diagnosis of neuritis and not infrequently escaping the suspicion of leprosy for months or years, in the hands of neurologists. Several cases have finally come to a diagnosis of leprosy when the skin evidences of macules or tubercles elsewhere have developed.

On the feet the bullæ seldom appear so early, and when they do come they are found on the plantar surface, usually going on to actual ulceration, trophic in character.

Late leprosy will develop bullæ as evidences of trophic changes and here the destruction of skin and deeper tissues is the rule, finally causing the destructive, amputative deformities found in nerve leprosy and the loss of terminal or intermediate phalanges of the digits of fingers and toes.

The tubercles in leprosy have their favorite location on the face, involving especially the lower part of the forehead, the ears, the nose, the chin, the cheeks, in the order named. The hands and other parts are less frequently involved.

They may begin in the patches of a macular eruption, or they may develop in normal skin. When sufficiently

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developed tubercular or nodular leprosy is essentially a bilateral, symmetrical disease. In some cases individual tubercles cannot be distinguished, but the whole skin of the face is greatly infiltrated, thickened and discolored, the surface remaining smooth, or, more often, cut by furrows sometimes a quarter of an inch deep in the natural lines of cleavage, or in the folds of the forehead, cheeks or chin. This furrowed type is especially marked on the cheeks and forehead and gives the leonine expression to the countenance more strikingly than the other varieties. In other cases the tubercles preserve their integrity, studding the face in their favorite areas of distribution with nodules varying in size from a pea to a marble. The color is usually a dusky reddish-brown, or may be waxy white in those cases in which the lesions are scattered and which are usually the most malignant. Each individual nodule is rounded at the base and spherical in contour, much as if peas or marbles had been stuck in the skin.

The eyebrows and beard may fall in this type, but as the scalp is not usually affected its hair may be preserved in its integrity until very late in the disease or to its termination.

Periodically in the course of the disease there may occur an outbreak of tubercles, evanescent in character, highly inflammatory and very painful. These occur during the course of the lepra fever before mentioned, which may last from one to five or six weeks, or even longer. These tubercles are deep-seated and dull red in color, not showing the brown pigment of the chronic type. They fade away with the subsidence of the fever and sometimes one crop will disappear to be replaced by another before the temperature returns to normal. The inflammation in this type is sometimes so intense that vesicles and bullæ develop on the tops of the tubercles, and some may even undergo suppuration with the formation of abscesses. Their distribution over the body is far more general than that of the permanent tuber-

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cles, as they occur not only on the face and hands but also on the trunk and on both the flexor and extensor surfaces of the extremities. The type of fever referred to as lepra fever is not the fever usually described as one of the prodromal symptoms of leprosy, but is an irregular elevation of temperature ranging from 100 to 104 F., and associated either with marked changes in the macules or tubercles present before the occurrence of the fever, or with the formation of such tubercles as have just been described. These tubercles may be especially recognized by their tendency to uniformity in size and their usual lenticular shape as if a flat bean were embedded in the skin.

The lepra fever has two distinguishing symptoms, the rise in temperature and the development of tubercles different in many characteristics from the lesions found as the usual evidences of leprosy. In the tubercular and mixed cases it occurs at varying intervals of time and is of varying duration, while in the pure anesthetic and trophic cases, as there are no tubercles, the skin evidences are lacking. Though there may be periodic rises of temperature, they are often associated with the suppuration which is the result of nerve disturbances and which is more liable to affect the bones and joints than the skin; in consequence the cardinal point in the diagnosis of lepra fever is lacking.

The inflammatory evidences in the tubercles accompanied by a general rise of temperature occur in almost every case of tubercular or mixed leprosy, though the symptoms are sometimes of so slight a character as almost to escape observation. The temperature may vary from so slight a rise above the normal as to occasion merely a feeling of malaise, to a grave febrile condition. The range of temperature is from 99 to 105 or 106, and two cases have been observed in which the result was fatal. The attack is often ushered in with a chill, and the duration is very variable—from a few days to several weeks or even months. Some patients have been known

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to have as many as three or four attacks during one year. The chief features of the temperature chart are the remittent character of the fever, and the sudden great rises and fall of temperature. The chart of a well-marked case very closely resembles that of septicemia.

The occurrence of marked inflammatory symptoms in old tubercles, infiltrated patches, macules, or in areas of skin which apparently were previously healthy, is coincident with the rise of temperature and is characterized by swelling, redness, pain and, rarely, suppuration. The occurrence is most frequent in old tubercles and least frequent in areas of skin which previously were not involved. The duration of the inflammatory nodules is short, but one crop is followed by another as long as the fever lasts. The location is most frequently on those parts of the body that are involved by the chronic characteristic nodules of leprosy, the face, neck, hands, and also the arms and legs. The distribution seems, like that of the chronic lesions, to prefer those parts of the body in which the temperature is lowest. The trunk is less frequently involved, and we have seen no cases involving the scalp. The number of lesions found at one time is very variable and they are disseminated with an irregular, bilateral symmetry. They vary from the size of a split pea to that of a hen's egg. The elevation above the surrounding skin is well marked and the nodules are of a globular contour, usually rounded in outline and distinctly limited in area. The color is uniformly red—a brighter and more brilliant hue than the dusky purplish red of the stationary tubercles, from which they can be differentiated not only by their inflammatory character but also by their rapid development, their evanescent character and an occasional tendency to suppurate and occur on parts of the body not usually affected by permanent bacillary deposits. Unless suppuration occurs the nodules are quite firm to touch and most resembles those found in erythema nodosum. It

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has been a matter of observation that often after attacks of lepra fever there has been improvement in the old tubercle and in the general condition, which seems to argue that during these attacks some bacillary product is formed which not only causes the elevation of temperature but also either directly affects the life or growth of the organisms, or indirectly, through the elevation of temperature, produces a condition unfavorable to the germ life.

In support of the latter view may be mentioned an observation made by Dr. F. B. Gurd, of the Department of Pathology of Tulane, in which the pus from an abscess caused by the suppuration of an inflamed tubercle was found to contain no organism except the bacillus of Hansen. These bacilli were found to be incapable of cultivation under the same conditions in which other Hansen bacilli had been found to flourish.

It is also interesting to note that during the administration of a series of hot baths, in which an effort was made to maintain an elevation of temperature of 104 for several hours, two tubercular cases developed lepra fever. If we may be permitted a little speculation, the great improvement derived from elevation of temperature, even in advanced cases of leprosy, may be explained on the hypothesis that the lepra bacillus does not thrive at high temperatures. The location of the chronic tubercles is very suggestive of this, as is also the improvement noted after erysipelas, lepra fever, and artificial elevation of temperature by means of hot baths. It seems possible that the products of the disintegration of dead bacilli provoke a general rise of temperature as well as the local heat of inflammation, and that the febrile condition thus produced reacts on bacilli in other locations, which, in turn, in their disintegration, liberate fever-producing toxins. It is conceivable that such a process should continue until all the less viable bacilli become destroyed, when the temperature returns to normal and old lesions show considerable improvement.

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With the exception of the tubercle associated with the lepra fever the nodules of leprosy seem to have a marked preference for the exposed parts of the head. The scalp is almost always free, while the ears are, on the contrary, almost always involved. They become enormously enlarged either by the presence of tubercles, in the lobes especially, or by a diffuse infiltration, both of which cause a marked discoloration. It is not unusual to find, even in terminal cases, tubercles present massed over the entire face and ulcerating, the limit of the most aggravated part of the eruption clearly marked by a line around the neck about where the shirt-band rests. On the trunk and arms and legs the macular eruption is far more common than the tubercular, though nodules may occasionally be found over a macular patch or even on a part of the skin presenting no other lesions. The tubercles never mass over the entire body as they do over the face. The most common condition on the hands is the thickening of the skin and pigmentation, with tubercles more sparsely scattered than on the face, the color being a dusky brown. The infiltration and swelling of the hands so affect the skin as often to cause a papery consistency like thin parchment.

The ulcers of leprosy are of two kinds, the perforating and the purely cutaneous. The latter occur most frequently on the face and on the legs. On the face they are usually superficial, but those around the mouth are liable to cause considerable destruction, and when the ulceration has healed the shrinking resulting from cicatrization will reduce the mouth to about one-third its normal size. The ulceration of the face occurs only in the terminal stage when the tubercles have become large and thickly aggregated, and it is found only in the tubercular and mixed types, the trophic form, or nerve leprosy showing in the face only by the infiltration of the whole mask of the face, with thinning of the epidermis, leaving the skin glossy and pigmented. The ears in this form are often flabby and pendulous; ectropion causes a stare,

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which is a peculiarity of this disease. The cause of the breaking down of the nodular masses seems to be done more to a disturbance of circulation in the skin than to the bacilli present, and this seems true also of the ulcers of the leg, where the circulatory balance is easily disturbed by gravity.

The perforating ulcer is associated only with the anesthetic form and is found only on the hands and feet, and more often on the ball of the foot than elsewhere. It is a surgical condition, being a sinus leading to necrotic bone. The horny layer of the skin is much hypertrophied when the ulcer is on the foot and the condition is painless.

A strong confirmatory symptom of leprosy is the anesthesia found in all types. In the tubercular type it is confined to the lesions, but in the anesthetic it spreads over the area of distribution of the nerve affected. The sense of pain and temperature are lost before the sense of touch, and in the anesthetic type the nerves most frequently involved first are the ulnars. The loss of sensibility begins usually in the tip of the little finger and spreads gradually to the adjacent fingers and up to the forearm. Other nerves become involved later on and the anesthesia may become general. In this instance there is always either marked thickening of the ulnar nerve or distinct nodes along the nerve. The left side is more often the first to be affected.

The mutilation in the anesthetic or nerve type is almost confined to the hands and feet, usually being limited to a loss of the fingers and toes, and is due to trophic changes caused by nerve destruction. The atrophy may be manifested by the "claw-hand," in which the flexor tendons and muscles shrink more than the extensor, drawing the fingers up and preventing extension, or it may affect the bones, causing either necrosis or a gradual degeneration and absorption.

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When necrosis occurs, a perforating ulcer is established and persists until the fragment of dead bone, sometimes an entire phalanx, is discharged. The ulcer then heals, leaving the finger or toe shortened by the loss of bone. When necrosis with suppuration does not cause the loss of bone in mass, a slower process of absorption goes on, and the flexed fingers become shrunken masses of flesh with atrophied nails at their extremities.

The curious condition of an amputation at the joints by constricting circular atrophy, just as in the disease known as "ainhum," is often observed and fingers and toes are often lost in this painless way. A band of fibrous tissue forms around some part of the digit and gradually constricts the underlying tissues. The band is usually about one quarter to one-half inch in breadth, and as it grows tighter the tendons and bones under it atrophy until the finger is left hanging by a fibrous band, which can easily be cut off with a pair of scissors; or, if left to itself, the finger will fall away, the patient often being unconscious when the loss occurs.

The suppuration attending the necrosis of bone may extend to joints involving the articulations at the wrists and ankles and occasioning a condition like tuberculous or septic arthritis.

Considerable attention has been directed to leprosy in the United States and recent cases have enforced the belief that not enough emphasis has been placed on the training of government physicians with regard to this disease. The notoriety attaching to the Early case alone, which excited the qualified criticism of at least two distinguished foreign leprologists, may be cited in point.

The United States has specific immigration laws which require the deportation of lepers; yet in 1908 several patients with advanced leprosy were shown in New York at the International Dermatological Congress, and some of these cases were in recently imported foreigners.

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Within the past three years Dr. Dyer has seen two lepers from Central and South America, who reached New Orleans by way of New York. These cases were well enough marked to have been recognized by any health officer who had even a meager idea of the disease.

It is highly important that the cardinal symptoms of leprosy should be learned by the officers of the public health so that importation of leprosy may stop. It does not require any more legislation, but more education of port physicians.

The salient points of diagnosis in leprosy consist in the recognition of the stamp of the disease, which is always suggested by the dusky hue, the swollen skin, the overhanging eyebrows and the raucous voice. The hands, too, have a thinned epidermis and an altered color which is different from that in any other disease. The presence of tubercles in the skin of the face, at the lips and about the nose, with others, in the pendulous parts of the ears—all these should make a case suspicious.

The different diagnosis of leprosy, clinically, is at all times simple. There are only two conditions which at all resemble tubercular leprosy, iodism and disseminated tuberculosis cutis. The first-named condition is seldom seen in the areas common to leprosy and the nodules of iodism are highly inflammatory and ready to break down.

With tuberculosis of the skin, the lesions are numerous, small, and deep-seated, under the epidermis as a rule. They are dirty white in color and seldom assume a reddened hue. Moreover, this condition on the face is unusual and when it does occur, the lesions are more apt to occur bilaterally and symmetrically, in numbers, on the cheeks and wings of the nose than elsewhere.

We would finally make the point that all physicians should report any cases of leprosy coming under their observation so that the actual occurrence of this disease

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in the United States may be studied and the statistics derived may be of some value in establishing an institution for the care of leprosy under government control and expense.

124 Baronne Street.

ABSTRACT OF DISCUSSION

DR. A. RAVOGLI, Cincinnati: It would be somewhat difficult to measure the value of fever as a diagnostic factor in these cases. The fever is usually present in the early stage of the disease, but we seldom see cases of leprosy in their development. We usually see them when they begin to suffer from neuralgic pains or during the eruptive stage. It is extremely difficult to establish the diagnosis of leprosy in the second stage, when the eruption which we call the leprides are developing, as they can easily be mistaken for various kinds of eruptions. The only characteristic symptom is when they show the toxic erythema—large, reddish patches on the arms or in other regions which usually are accompanied by severe neuralgic pains when the nerves have become involved. In the later stages, when the tubercles form, the disease is more readily recognized. I have seen cases where there was scarcely any eruption—merely spots of cloasma or vitiligo and neuralgic pains. Then the hands begin to be paralyzed and take on that peculiar appearance, hand-drop. In one case only a large leproma developed on the knee and another on the foot, causing ulcer which involved the joint and the bones. I firmly believe that with a little experience and attention it will not be difficult to establish the diagnosis of this disease, which should be stamped out. This is being done with brilliant results in Norway. In the United States we have about 278 cases, some in North and South Dakota from Iceland, some in Minnesota from Sweden and Norway, some in Louisiana from the Bahama Islands, some in San Francisco from the Orient, and other scattered cases here and there. It is important, I think, that the United States Government should take up this question. We had a case in one of the hospitals in Cincinnati, in which the diagnosis of leprosy was fairly positive. The patient was a negro soldier who had spent four years in Cuba, and when we asked the health officer of the city what to do with him, we were told to let him go. I think it is dangerous that these patients should be allowed to remain in localities where they will be in free communication with other people.

DR. MARCUS HAASE, Memphis, Tenn.: I would not have had the opportunity of seeing a case of leprosy had it not been for this lepra fever. I would like to ask Dr. Dyer what percentage of these patients have this fever after the disease is fully developed?

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DR. S. T. DARLING, Ancon Hospital, Canal Zone: The subject of leprosy is a very important one in the United States at this time when soldiers who have served in the Philippines and where employees from the Canal Zone are returning to take up permanent residences in various parts of the country. In the Canal Zone we have had no case of leprosy among Americans, and but one in a European. Our quarantine officers have been alert and active in the detection of the cases passing through their hands. We find that the diagnosis of the nodular form of the disease is easy. In fact, several of our cases have been detected by district sanitary inspectors, who are laymen. The anesthetic type of the disease presents greater difficulties. In these cases it is important and necessary in the examination to strip the patient and look for the presence of the characteristic annular areas of anesthesia and discoloration of the skin on the back, breast, abdomen and buttocks. These cases frequently present circular ulcers on the feet between the second and third toes. We have at times removed parts of the enlarged ulnar nerve for diagnosis and failed to detect bacilli. The *x*-ray as a diagnostic aid has been used by Dr. A. B. Herrick, Ancon Hospital, for in association with trophic ulcers of the feet in the anesthetic type there is a definite atrophy of the phalanges near the ulcer, which is well shown in radiographs. I believe Scheube has called attention to the fever of leprosy, but I do not think it is of much importance in the diagnosis of cases of leprosy of the anesthetic type.

DR. WILLIAM LITTERER, Nashville, Tenn.: I was greatly interested in Dr. Dyer's explanation of the fever in leprosy. I think he is correct when he states that it is due to some form of intoxication. While I do not know whether it is feasible, I would suggest taking an emulsion of the lepra bacilli after their growth on a proper medium and injecting the bacilli as a means of treatment.

DR. I. DYER, New Orleans: I again wish to make the statement that my paper was not an academic presentation of the subject, but rather a discussion of its salient features, because of the evident ignorance of the disease in our own country. Drs. Duval and Gurd, the pathologists of Tulane College, intend to present to the Society for the Study of Tropical Medicine a culture of the lepra bacilli which they have successfully carried on since last December, and we have already considered the elaboration of a vaccine. We hope, before another year has gone by, to have something to report in that line. In my paper, I purposely omitted any discussion of the subject of the laboratory diagnosis of leprosy. The discussion of anomalous types of the disease is largely covered in the portion of my paper which I omitted in reading. With us, and in all countries where the disease is fairly virgin, the anesthetic

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type is much more difficult to recognize than the tubercular. Such cases have been mistaken for syringomyelia by neurologists.

With reference to lepra fever, we have considered only that fever which occurs after the disease is well defined, and not that observed in the prodromal stage. In most of the cases of skin leprosy, which we have termed the tubercular type, this fever is often observed after the disease is well developed. As these cases have improved—and fully 90 per cent. of our cases have undergone a high degree of amelioration—the fever has always been associated with the improvement. In Louisiana, leprosy has been recognized and demonstrated since 1778.

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HAIRY OR BLACK TONGUE

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The subject of hairy or black tongue has engrossed a varied degree of attention in dermatologic literature. A comparatively large number of the cases, chiefly from French and English sources, were reported at the time of the discovery and early mention of the affection. Brosin[1] recorded some forty odd cases reported prior to 1888. The next large increment of cases occurred when investigators first took issue in regard to its parasitic or non-parasitic nature, which has remained a more or less unsettled point of contention to the present day. Relatively few cases have been reported in recent years, not so much because the affection is possibly more rare or exceedingly infrequent as because little additional information could be offered regarding its etiology, pathology and treatment. There are scarcely a hundred cases recorded in the literature at the present time, and if the spurious and unauthenticated cases were eliminated the remainder would probably not total much more than half that number. The earliest report of the affection probably emanates from Rayer,[2] who in 1835 described, under the name "discolorations pigmentaires," several cases of black discoloration of the dorsal surface of the tongue. Eulenberg[3] in 1853 described a black-coated

1. Brosin: Monatsh. f. prakt. Dermat., 1888, vii, No. 1, Ergänzh., p. 5.
2. Rayer: Traité théorique et pratique des maladies de la peau, 1835, iii, 573, article Nigrité.
3. Eulenberg: Arch. physiol. Heilk., 1853, xvi, 490.

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tongue (*eine schwarze Zungenbelag*) in a 2-year-old child affected with diarrhea, which persisted for several months. He first called attention to involvement of the filiform papillæ, a feature more carefully elaborated later by Gubler.[4] St. Germain[5] in 1855 reported some transient cases of short duration in debilitated individuals, under the name "nigrité de la langue." Raynaud[6] in 1869 independently described several cases as a new affection, and first ascribed to the condition a parasitic cause. He pictured mycelia and spores, unlike any previously described. As soon as Raynaud attributed a parasitic etiology interest in the affection materially increased; Gallois[7] was unable to confirm Raynaud's observations, and Richter[8] states that he had observed the tongue epithelium to develop into thick, black, cylindrical "turf" (*Rasen*) without ever being able to discover Raynaud's fungus. Féréol[9] likewise found no evidence of spores in his case, and stated that their presence in hairy tongue must be of accidental rather than etiologic character. He considered the hypertrophy of the filiform papillæ the essential pathologic feature, and called the affection *l'hypertrophie épithéliale filiforme*. Within a few years Laveau,[10] Lancereaux,[11] and Dessois[12] reported some cases with which they confirmed Raynaud's parasitic etiology. Dessois attempted to confirm the parasitic nature of the affection by inoculation experiments on his own tongue, which, however, proved negative in character. He named the affection *glossophytie*. Rayer reported that not only were inoculation experiments negative, but morphologically similar spores

4. Gubler: Bouche (Séméiologie) Dict. de Dechambre, 1869; quoted by Brosin: Note 1.
5. St. Germain: Compt.-rend. Acad. d. Sc., 1855, March 28.
6. Raynaud: Séance de la Soc. med. d. hôp., Feb. 26, 1869.
7. Gallois: Séance de la Soc. de Biologie, Aug. 7, 1869.
8. Richter: Krankenmachende Schmarotzepilze Schmidt's Jahrb., 1871, cli.
9. Féréol: Séance de la Soc. méd. d. hôp., June 25, 1875.
10. Laveau: De la langue noire, Thèse de doctorat, Paris, 1876; quoted by Brosin, Note 1.
11. Lancereaux: Séance de la Soc. méd. d. hôp., Dec. 8, 1876.
12. Dessois: De la langue noire, Thèse de doctorat, Paris, 1878; quoted by Brosin, Note 1.

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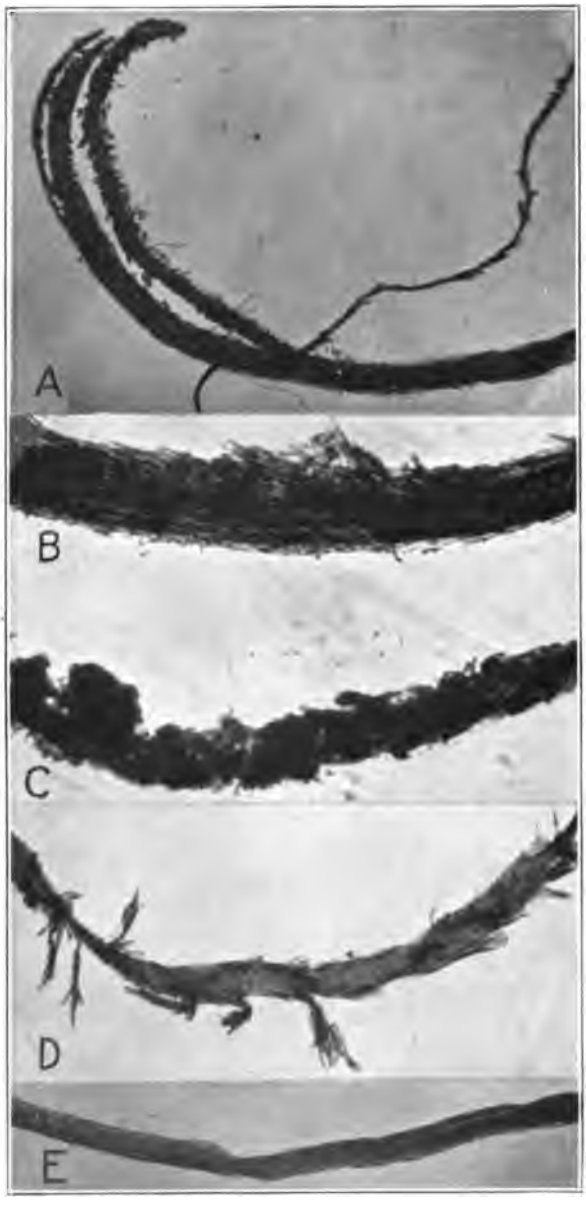

Fig. 1.—Specimens from patient with hairy or black tongue: A, separated from each other at the extremity; appearance, tuft-like; a single hair composed of several closely united shafts; B, stained hair of considerable size; C, unstained filament coated with loose masses, composed largely of micro-organisms; D, hair resembling in appearance a stalk of Indian corn; E, one-half of hair measuring ¾ inch; tenfold magnification.

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Fig. 2.—Hair-like filaments cut vertically and longitudinally to their long axis. Many interwined filaments cut obliquely and transversely. Filaments reach upward and forward in irregular parallels.

Fig. 3.—Papilla-like bodies within the rete Malpighii; probable origin of hair-like filaments.

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were present on normal tongues. Pellarez,[13] a Spaniard, erroneously regarded the condition as a vegetating growth and Salter[14] ascribed the discoloration to an anomaly of pigmentation. Butlin[15] believed the fungi normally found in the mouth could, under special conditions, impart a black discoloration to the coating of a tongue. Schech[16] described the discoloration under the microscope as light to dark brown and diffusely distributed over the hairs, without being interspersed with sharp, distinct accumulations of pigment or areas free from pigment. The hairs consisted of thickly crowded masses of long, thin epidermic cells, with a marked tendency to bristle and branch at the borders. They set forth the greatly enlarged, cornified and pigmented filiform papillæ. A remarkable feature was the absence of fine granular masses of cocci, bacilli and leptothrix, which are a part of the normal coating of the tongue. Schech found no evidence of fungi in support of Dessois and Sell and was obliged to retract his former expressed views regarding its mycotic character. Brosin[1] regarded the affection as a hypertrophy of the papillæ filiformes, with abnormal pigmentation and keratosis of the affected tissue. This view was supported by Rosenberg,[17] Rydygier,[18] Wollerand,[19] Surmond,[20] and others, and their studies revealed the presence of many forms of micro-organisms of incidental and non-pathogenic significance.

Those who have confirmed the parasitic nature of the affection in more recent years are Roth,[21] who found a

13. Pellarez: Gaz. méd. de Paris, 1879, No. 52 (abst.).
14. Salter: Todd's Encylopedia of Anatomy and Physiology, 1852, No. 6.
15. Butlin: Diseases of the Tongue, 1885, p. 31.
16. Schech: München med. Wchnschr., 1887, No. 14, April 5.
17. Rosenberg: Quoted by Mourek: Arch f. Dermat. u. Syph., 1894, xxix, 369.
18. Rydygier: Beitrag zur selteneren Erkrank. der Zunge, Arch. f. klin. Chir., 1891, No. 41, p. 767.
19. Wollerand: Sur la langue noire papillaire, Virchow's Arch. f. path. Anat., xxv.
20. Surmond: La langue noire, Gaz. d. hôp., 1891.
21. Roth: Wien. med. Presse, 1887, p. 935.

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micro-organism abundantly present in two cases, to which he attributed the discoloration, and called the affection a keratomycosis. Dinkler[22] disclosed the presence of a filiform bacillus, but was unable to cultivate it. Lake[23] detected the presence of round spores. Ciaglinski and Hawelke[24] and Senziak[25] were able to cultivate a black fungus to which they attributed etiologic importance, but only at room—not at body—temperature. Rostowjew[26] describes in his two cases, in addition to the ordinary mouth bacteria, a peculiar cladothrix, the cultures of which were black. Much infectious significance is attributed by Rostowjew to the occurrence of the affection in husband and wife. Gottheil[27] illustrates the spores in his case, which showed only a black discoloration of the tongue, without a coat of hairlike prolongations. Lucet[28] describes the presence of small round or oval double contoured, highly refractive bodies, with hyaline or finely granular contents. They stained with compound solution of iodin and grew luxuriantly on 5 per cent. glucose agar at 37 C. Inoculation experiments on rabbit tongues were negative. Gottheil named the fungus *saccharomyces linguæ pilosæ*. Gaston and Laselet[29] believed that the cause of the black discoloration was a fungus which they successfully cultivated. Guéguen[30] is the latest observer to attribute this affection to a hitherto undescribed organism, the *Oospora lingualis*. Equally large is the number of present-day observers and investigators, who either ignore or regard as untenable the theory of the parasitic origin of the affection

22. Dinkler: Ein Beitrag zur Pathologie der sogenannten Schwarzen Haar-Zunge, Virchow's Arch. f. path. Anat., cxviii.
23. Lake: Black Tongue, Brit. Med. Jour., 1891, p. 946.
24. Ciaglinski and Hawelke: Beitrag zu einer seltenen Erkrankung der Zunge, Ztschr. f. klin. med., 1893, xxii, 626.
25. Sendziak: Beitrag zur Etiologie der sogennanten Schwarzen-Zunge, Monatsh. f. Ohrenh., 1894, xxviii, 112.
26. Rostowjew: Hospitals. Botkin, 1896, No. 8.
27. Gettheil: Arch. f. Pediat., 1889, p. 255.
28. Lucet: Arch. de parasitol., May 20, 1901.
29. Gastou and Laselet: Tr. de Soc. Franç. de dermat. et de syph., March 18, 1909, xx, No. 5.
30. Guéguen: Arch. de parasitol., 1909, xii, No. 8.

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and attribute it to other causes. Levisseur[31] attributed the cause in his case to use of silver nitrate and chromic acid in the treatment of syphilitic plaques. Schnabel[32] and Schourp[33] regard the affection as a common one among syphilitics, dyspeptics and tobacco users. Audry and Dalous[34] and Hallopeau[35] have observed the affection in cases of Darier's disease. Mourek,[36] in his carefully reported and investigated case, states that microorganisms were found sparingly and gave no evidence of anything of characteristic significance. The bacteriologic investigation was of negative character. He believed the process is a hyperkeratosis and the discoloration the result of contact with food and other extraneous products. The epithelial cells cohered and became mechanically discolored, as in other keratotic affections of the skin. Vollmer[37] states that though the etiology and mode of production is obscure, he is of the opinion that syhilis, mercurialization, strong disinfectants, tobacco, etc., are predisposing factors. He regards the parasitic etiology as untenable.

REPORT OF CASES

CASE 1.—On May 25, 1909, Mr. A. D., aged 85, was referred to my attention for a peculiar discoloration of the tongue, which was the site of severe subjective pain and discomfort. Examination revealed a brownish-black discoloration extending anteriorly from the circumvallate papillæ to within almost one inch of its tip, and one-half inch of the right lateral border. The affected area was irregularly elliptical in outline, situated for the most part on the right side of the tongue, but slightly transgressed the median line at its middle third. The patch was black at its center with borders that gradually faded from brownish-black to yellowish-brown. The remainder of the tongue and the mucous membranes of the mouth were

31. Levisseur: New York State Jour. Med., 1899, xlix, 42.
32. Schnabel: Haar-Zunge, Inaug. Dissert., Leipzig, 1904.
33. Schourp: Monatschr. f. Harnkr. u. sex Hyg., iii, No. 2.
34. Andry and Dalous: Jour. de mal. cutan., 1904, xvi, 801.
35. Hallopeau: Ann. de dermat. et. de syph., 1896, series 3, vii, 744.
36. Mourek: Arch. f. Dermat. u. Syph., 1894, xxix, 369.
37. Vollmer: Arch. f. Dermat. u. Syph., 1898, xlvi, 13.

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bright red and normal in appearance. Salivation was very marked, and the patient complained severely of intense pain in the tongue, which was also referred to the ears. The patch was thickly covered with a soft, felt-like coating of hair-like processes, which on more careful examination and inspection were found to be inextricably interwoven and matted together. in the manner of "a field of grain laid low by storm and wind" as previously described by Gubler, Raynaud, Stokes and Lake. An abundance of long hairy filaments, some of which measured ¾ of an inch in length, could be readily removed with thumb forceps. The patient, an intelligent German, stated that his personal attention was first directed to his tongue, some two months prior to the time of the examination, by pain and a sense of soreness in the tongue, and the black discoloration was then in evidence in its present unchanged form. No history of its incipiency or probable duration was obtainable.

Biopsy.—On May 28 a biopsy was made for histologic study. Patient was observed daily. The pain became more intense and salivation more marked. On June 3 a marked swelling manifested itself at the left lateral border of the tongue near its middle third and remote from the hairy involvement; the mass, which was deep-seated in origin, was firm and hard in consistence, irregular in outline. The lesion was diagnosed as an epithelioma and the case referred to a surgeon. The subsequent history confirmed this diagnosis. As soon as ulceration took place the patient experienced some sense of relief from his distressing pain. On Feb. 15, 1910, the bed-ridden patient was still alive, although the disease had made great inroads on his previous fairly robust constitution; death eventually took place March 5, 1910. The complicating malignancy in this case was, without question, a mere coincidence, and has its analogue in a case of a 49-year-old brickmaker, reported by Lediard, who had an epithelioma at the tip of the tongue remote from the pathologic hairy area.

Case 2.—R. K., aged 19, was first seen in consultation April 6, 1905. Patient stated that three months previously he noted an abnormal sensation in the tongue, resembling the presence of a foreign body on the surface which could not be dislodged. On looking into a mirror he noted for the first time the black discoloration, became alarmed and forthwith brought the condition to the attention of his physician. The examination revealed an intense blackish discoloration of the tongue, with borders imperceptibly fading to brownish-yellow, occupying a triangular area, extending from the circumvallate papillæ anteriorly along the median dorsal surface of the tongue almost

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to its tip and lateral borders. The same soft felt-like coating of matted hair-like processes was observed as in the previous case, and a specimen was removed and preserved in alcohol for histologic examination. Pain and distress were entirely absent, and there were no subjective symptoms except as already noted. Patient was last observed in Jan. 15, 1910, and during the intervening five years no appreciable change was detected in the clinical appearance of the tongue. Patient persistently refused a biopsy, but readily permitted the removal of large numbers of hairy processes, some of which measured fully ¾ of an inch in length. Syphilis was absent and there was no history of drug-taking, or the use of caustic or astringent applications.

In addition to these two well-defined clinical cases it has been my privilege to observe several cases of less marked character in connection with conditions of general dermatologic interest. The patients were, almost without exception, unaware of or at least indifferent to the manifestations on the part of the tongue, which were revealed merely by process of routine examination, and doubtless would have been dismissed with passing notice had not the unusual interest of the condition been understood. In most cases there was at least a moderate amount of felt-like covering, of hairy growth, in addition to the brownish or blackish discoloration, and hairs from ⅛ to ¼ of an inch could be readily removed and floated in water or alcohol. In some cases there was mere discoloration without an associated hairy growth, as reported by Gottheil, Stokes, Ciaglinski and Hewelke and Sendziak. This discoloration was soft, mushy in character, and could be freely but somewhat incompletely removed by light scraping. The cases occurred for the most part in early syphilitics and were observed in the process of the examination of the tongue for the presence or absence of mucous plaques, or the coated or non-coated state of the tongue in non-syphilitics. All of the cases occurred in males. Most, but not all, of the syphilitics were using at the time astringent and antiseptic mouth lotions. The patches disappeared, however,

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in some of these cases, in spite of the persistent use of the astringent antiseptic mouth lotions.

One patient, affected with gonorrhea but not with syphilis, was taking sandalwood oil internally, but the patch persisted for some time after the internal administration of the oil was withdrawn. It disappeared entirely after a lapse of several months.

In two cases syphilitic infection was of long standing; one patient had an extensive leucoplakia of the tongue and these areas were free from the yellowis-brown discoloration, which occupied an irregularly oval area near the center, anterior to the circumvallate papillæ. Most, but not all, of the cases occurred in patients who used tobacco immoderately. Dietary indiscretions and gastro-intestinal disturbances were in evidence in the majority but not in all of the cases. The patches were evanescent and transient in all the cases, fading or disappearing without treatment and attention, and occasionally relapsing from untoward local or general influences. These cases lacked the clean-cut clinical characteristics of the first two well-defined cases, in which the color was more intense, the hairs longer, more numerous and interwoven, the patches thicker, more fur-like and sharply defined and more persistent and stable in character. I am inclined to believe that several of the cases reported in the literature belong to this second class of—if I may be pardoned the term—spurious or pseudo cases.

Microscopic Examination.—The microscopic appearance of the hairy-like filaments was fairly constant, when compared with each other and with those described in the literature. Specimens from the pseudo—or spurious—cases could not be differentiated microscopically, except for length and thickness, from those of the two well-defined ones. Specimens unstained and stained by various methods were examined; the unstained specimens, for the most part, showed a more regular and better preserved outline. The color of the unstained specimens is a diffuse yellowish-brown—as already noted by Schech, Mourek, and others.

The outline is an elongated cylinder, hair-like in general appearance. The resemblance to a hair is accentuated in many

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instances by the presence of a zone analogous to the medullary canal. In many there are several of these zones of varying color intensity, and on close examination they are found to owe their presence to the fact that a single filament is often composed of two or more closely united shafts. These shafts are united the greater part of their entire length; they become separate and distinct from each other a short distance from the distal extremity, imparting a peculiar tuft-like appearance, not altogether unlike that observed in a pineapple (Fig. 1 A). Occasionally one of the united shafts will become dissociated at some more median point, and impart an appearance not altogether unlike that of the leaf to a stalk of Indian corn (Fig. 1 D). The resemblance to Indian corn becomes more marked if there are several lateral dissociations.

Lateral deviations have been noted by Schech and other early observers. On closer examination under higher magnification the filaments are observed to be composed of thin, non-nucleated, stratified, closely superimposed epithelial cells. Their cornified, non-nucleated character can be confirmed if the filaments are macerated with gentle heat in a solution of potassium hydroxid. The individual cells are superimposed in such a way as to produce serrated borders; the serrations are constantly directed downward, producing a peculiar tesselated effect, which can be compared to the scales on the surface of a pineapple. This imbricated character has been frequently noted in the literature; it is not marked enough to conjure up the resemblance of a row of inverted funnels, as described by Brosin, nor is their order, as he states, ever reversed, so that they partake of the appearance of a harpoon or trident. For similar reasons the spike-like appearance or resemblance to the head of a wheat-stalk described by Mourek, is not to be discerned; surface indentations were not observed to recall the "corncob" effect described by Levisseur. The serrations at the border are directed toward the base, and away from the rounded and cleft extremities constantly enough to permit a ready differentiation of the distal from the proximal extremity.

In well-stained specimens the filaments were observed under oil-immersion to be thickly studded with masses of cocci, which morphologically resembled the common pus germs. They were present in exceedingly large numbers, were intracellular and extracellular, and often in such density as to resemble pure cultures of the common staphylococci. Larger and more deeply stained cocci and diplococci were interspersed here and there together with bacilli, leptothrix, and various forms of organisms commonly found in the mouth. In addition to the various stained micro-organisms, a few large round, highly refractive, double contoured bodies, some larger, some smaller,

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often in such proximity as to impart a budding character, were observed here and there in most of the specimens examined. They were not numerous enough to assume pathogenic importance, and to all appearances their presence partook of a coincidental character. Some unrecognizable fungi and micro-organisms were also observed; the micrococci, however, predominated greatly over all other forms.

Culture Experiments.—Culture experiments were attempted in both genuine and spurious cases. The affected surfaces were carefully sponged with ether and 5 per cent. glucose agar: nutrient agar and blood-serum were carefully inoculated with removed filaments and platinum loop inoculations from the affected area. Some of the cultures were kept at 38 C.; others at room temperature.

The cultures uniformly remained sterile or became the seat of innumerable, small, glistening, white, superficial colonies, which morphologically and microscopically resembled in every particular *Staphylococcus albus*. No fungus was evident even on prolonged standing in any of the cultures examined.

Histology.—A biopsy was obtained only in Case 1, and the histologic report with accompanying illustrations, is the first, to my personal knowledge, to be recorded for the affection. Under low power the filaments when cut vertically and longitudinally to their long axis, are observed to reach upwardly and forwardly in irregular parallels Fig. 2). Many of the intertwined filaments are cut transversely and obliquely. The filaments preserve for themselves a feather-like appearance. When cut transversely to their long axis their continuity is preserved only a short distance and most of them appear as small round or oblique fragments. The filaments can often be directly traced to their origin from papilla-like projections of the stratum corneum. The stratum corneum elongations promptly take on a fringe of serrated, more loosely arranged and deeper staining cells; they often coalesce within a short distance of their proximal extremities with one or more adjacent filaments to form double, triple, or quadruple filaments. Acanthosis is another marked pathological feature. The rete and the papillæ are considerably hypertrophied, and there is a very extensive downward proliferation of almost every fourth, fifth or sixth interpapillary process of the rete Malpighii. The lower layer of columnar cells is sharply defined, well preserved and in a state of active proliferation. The pars papillaris and subjacent tissue are entirely devoid of any marked pathological change save a diffused, mild infiltration of inflammatory products, the distribution of which is limited almost exclusively to the pars papillaris.

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Fig. 4.—The same papilla-like bodies cut transversely and imparting the appearance of epithelial nests clustered in circles.

Fig. 5.—Superficial origin of the hair-like filaments.

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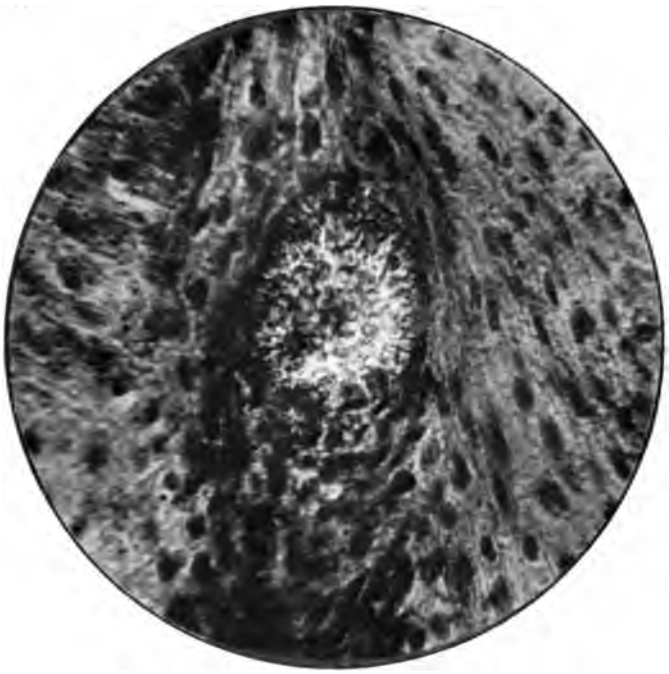

Fig. 6.—Blood cavity strongly magnified, showing its intra-epithelial position. Cavity is lined with a layer of endothelial cells.

Fig. 7.—Small blood cavity within the epidermis with areas of edematous and degenerated epithelial cells at the rete papillary border.

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One of the most striking pathologic changes, and possibly second in importance only to the filaments, is the formation of papillæ-like bodies within the rete Malpighii (Fig. 3). They are differentiated from the rete, in which they are situated, by a well-defined layer of more deeply stained columnar basal cells. Their well-defined interpapillary spaces are devoid of fibro-connective tissue and filled with epithelial cells of the rete. They are further differentiated from normal papillæ by their diminutive type. If cut obliquely or on cross section they partake of the appearance of epithelial nests (Fig. 4); and it is not unusual to note six to twelve or more of such nests clustered in a circle. If cut longitudinally they can be traced directly to the surface to points where the filaments take their origin (Fig 5). Having assumed that these intra-epithelium-placed papillæ are the origin of the hairs, I have termed them "epithelial founts."

The stratum corneum is more or less imperfectly preserved. In some places it is of normal thickness, structure and staining properties and covers a fair extent of surface. In places it is almost entirely lacking, and, when present, rises perpendicularly from the surface to form the proximal extremities of the hair-like filaments. Where it is preserved, it is often covered or partially covered with a thick layer of partially stratified, nucleated epithelial cells. Groups of degenerated cells are occasionally observed at the tips of the papillæ, or in the epidermis near the papillary border (Fig. 6). These cells are often surrounded by a single layer of endothelial cells; their yellowish color, small homogeneous appearance, angular outline, with interspersed darkly-stained lymphocytes, indicate that they are blood accumulations. Inasmuch as such accumulations have been observed and recorded in the corneous substance of cutaneous horns by Joseph and others, the analogy is plausible. These "blood cavities" and the rete-papillary border occasionally contain large rounded, hyaline or faintly granular, double culture bodies, which are apparently cell degenerations, rather than pathogenic spores, although they bear a morphologic resemblance to spores to which pathogenic importance has been attributed (Fig. 7). They are often embedded in a mass of large, edematous, vacuolated cells situated at the papillary border of the epidermis, which resemble the degenerative cell changes in Paget's disease.

The pathology cannot be dismissed without a brief comparative reference to cutaneous horns, ichthyosis hystrix, leptothrix and hair. The histopathologic similarity which some of these affections bear to hairy tongue is remarkable to the degree with which their clinical

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characteristics are dissimilar; and *vice versa,* the affections which preserve the greatest degree of clinical resemblance show the least histopathologic resemblance. Cutaneous horns, which have clinically little or nothing in common with hairy tongue, have much in common pathologically. They are composed of masses of cornified, or at least partially stratified, epithelial cells, arranged with wonderful cohesion into dense elongated columns, row after row separated by valley-like clefts, resembling the medullated canals of hair. Intra-epithelial spaces containing blood are also observed. The origin is purely epidermal, and the base rests on and apparently is developed from intra-epithelially placed papillæ and interpapillary processes resting above the area of the true papillæ, and true interpapillary processes, unless the latter, have disappeared from pressure atrophy. The former papillæ and inter-papillary processes correspond to the intraepithelially placed "epithelial founts" of hairy tongue.

Ichthyosis hystrix, which preserves possibly more clinical than histopathologic resemblance to hairy tongue, preserves little histologic similarity except a marked hyperkeratosis. The hyperkeratosis, however, is arranged parallel rather than perpendicularly to the surface and the spinous processes are the result of keratotic accumulations, spread irregularly over the surface of four or five hypertrophied papillæ. The inflammatory exudate is more perivascular, less diffused in character and more circumscribed to the capillary vessels of the pars papillaris.

Leptothrix, which has little or nothing clinically in common with hairy tongue, shows a striking resemblance under the microscope, in that the affected hairs are coated with an accumulation of loosely adherent cells and detritus, containing myriads of micrococci and other micro-organisms. The morphologic resemblance, under the microscope, of hair affected with leptothrix to the

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filaments of hairy tongue is very striking. An additional point of resemblance is the discoloration, which in leptothrix is often yellow or red, and in hairy tongue, black, to brownish-yellow. Pathogenically there can be little in common in the two affections. The *gross* clinical resemblance which filaments bear to hair is striking enough and give the affection a misnomer. Remarkable in many of its microscopic features, the resemblance is microscopically and histopathogenically a paradox that requires no comment. In origin, development, essentials of structure and pathogenesis they naturally share nothing in common with hair.

GENERAL DEDUCTIONS

Hairy tongue can be conveniently divided into two general classes: (1) true, idiopathic, or genuine cases, characterized by well-defined stable, black-brown or yellow-brown, thick, soft, fur-like patches covered with densely intertwined hair-like filaments, easily measuring from ¼ to ½ inches in length; and (2) false, pseudo or spurious cases, characterized by thickish, yellow-brown or greenish discolorations, of unstable evanescent character, covered with a soft mushy detritus, occasionally containing short filaments measuring ⅛ to ¼ of an inch in length. The true cases owe their origin to some anomaly of development, probably of congenital nature, in the sense that the germinal products from which they are developed are present from birth, but do not undergo growth and developmental changes until early adolescence or some later period in life. Such an origin is assumed and very generally conceded for moles, vascular, pigmented papillomatous and unilateral nevi, cutaneous horns,[38] etc., and can be extended with equal propriety to this affection, all the more since the histopathology reveals an anomaly of development (whose striking similarity to cutaneous horns has already been alluded to) rather than any evidence of an infectious or

38. Philip: Monatsh. f. Prakt. Dermat., 1904, xxxix, 630.

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inflammatory nature. An anomalous development and congenital origin is further evidenced by the fact that the true idiopathic or genuine cases are of stable character, and remain unchanged in size and form for indefinite periods, and localized to definite areas. Such would not likely be the case if they were of infectious origin or of inflammatory character resulting from local or general causes.

The pseudo or spurious cases are unstable and evanescent and probably owe their origin to such local or general irritating and infectious causes as tobacco, antiseptics, astringents, syphilis, etc. The presence of the filaments is probably due to an inflammatory hypertrophy of the papillæ filiformes. These cases in varying degree of intensity can be frequently noted, particularly in the early stages of syphilis, and constitute no uncommon affection. The diagnosis can be easily confirmed by removing some of the grumous coating of discolored tongues by means of a pair of fine forceps, and floating it in clear water or alcohol. The hair-like filaments can then be readily seen with the naked eye. The majority of the cases recorded in the literature probably belong to this group.

A parasitic origin for the affection could not be established on either clinical, histopathologic or bacteriologic grounds; it does not develop or spread clinically like a parasitic affection. Inoculation experiments were negative in the sense that the affections could not be distributed to other unaffected parts of the tongue. It failed to spread to the abrasions and excoriations of an intercurrent cancer of the tongue. The histopathology reveals chiefly anomalous structural changes, and the absence of the marked inflammatory changes generally incident to chronic and acute infectious and localized irritations. The fundamental abnormality is the presence of abnormal papillæ, and interpapillary processes or "filament founts" situated within the epidermis, from

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which the abnormally elongated, stratified and keratosed filaments trace their direct origin. Some of the basal cells at the papillary-rete border showed vacuolated and edematous change, to which, however, no special significance could be attributed. The filaments were freely studded with micro-organisms which resembled *Staphylococcus albus* morphologically, to which likewise no special significance could be attached. A few double-contoured bodies were occasionally observed among the filaments and in the deeper structures, to which no important significance was attributed. The bacteriologic findings were, as already stated, sufficiently negative in character to preclude, in my opinion, a parasitic etiology for the affection.

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PRIMULA DERMATITIS

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That the primula or primrose, a flowering plant found in many homes as a floral decoration, is frequently the cause of a dermatitis of more or less severe degree, is a fact not sufficiently recognized by the medical profession.

In this country attention was first called to the poisonous property of the species of primula known as *Primula obconica,* by J. C. White[1] in 1889 and again in 1890, when several cases observed in florists were reported.[2] With the exception of case reports by Denston[3] and Sweet,[4] there have been no further contributions to this subject by American writers, and in the consideration of dermatitis venenata in the latest dermatologic text-books the primula is either omitted entirely or is barely mentioned. This is in marked contrast to the large number of articles on this subject which have appeared in recent years, especially in English and German medical and botanical journals. The distribution of the primula in American homes is almost universal during certain seasons, and is certainly as wide-spread as in England and on the Continent, thus giving an equal opportunity for the development of cases. The discrepancy in the number of cases reported in this country is therefore perhaps attributable to a lack of

1. Garden and Forest, 1889.
2. Boston Med. and Surg. Jour., 1890, p. 425.
3. Med. Summary, 1903, p. 227.
4. THE JOURNAL A. M. A., July 27, 1907, p. 329.

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appreciation of the primula as the possible cause of some forms of dermatitis remaining grouped under the term eczema. I venture to assert that a more wide-spread knowledge of the toxic properties of this plant will shed light on the etiology of many instances of so-called recurrent "eczema," and of cases of "mild erysipelas," basing this on my experience following the presentation of a case of primula dermatitis before a local medical society in 1903. For some time thereafter I was frequently informed by general practitioners of the discovery of cases of primula dermatitis which had masqueraded unrecognized under the convenient term of eczema, (until the primula as a possible causative factor had been brought to their attention).

My personal experience with the dermatitis produced by the primula would indicate that it is not at all infrequent, as it comprises some forty or fifty cases, of all grades of severity and extent, observed during the past seven years. In addition I have learned from others of the existence of many instances of this affection, so that I now constantly hold the primula under suspicion when inquiring into the cause of a dermatitis. In this connection the remarks of Jadassohn[5] are very pertinent, when he says:

> In the past few years the best known—but still not sufficiently well known—inflammations have been those produced by some species of the primula in individuals with an idiosyncrasy toward this plant, affecting especially the hands and face (even with iritis), constantly recurring in acute form or appearing in a more chronic manner with exacerbations. Whoever has once experienced how much an "eczema" for years always appears at a definite time, tortures the patient, is treated unsuccessfully by all possible methods, subsides on rest in bed, and immediately reappears when the patient again goes about (because the care of the plant is resumed), and finally disappears entirely after disposing of the primula, will never again forget to search for the most varied external causes in eczemas of every description.

5. Deutsch Klin., x, 146.

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TYPES OF PRIMULA DERMATITIS

From the observation of any considerable number of cases it is apparent that the dermatitis caused by the primula presents itself chiefly in three types, depending on the degree of idiosyncrasy. Those possessing a well-marked idiosyncrasy to the toxic principle respond with an intense inflammation, erythemato-vesicular in character, at times with the formation of bullæ, and accompanied by more or less swelling. Others develop an erythemato-vesicular or erythemato-squamous eruption of a less acute type, with considerable infiltration, after repeated attacks, and scaling continued over a long period. Again, in others an intensely itching or burning sensation confined to the pulps of the fingers, which are puffed, tense, and slightly reddened, may be the only evidence of reaction.

The clinical picture of the highly inflammatory type in all its details is well presented in the following notes from the case of a housewife, aged 58 (?) made when the attack was of sixteen hours' duration.

On the face, from level of zygoma to border of jaw, are blotchy, irregularly outlined, erythematous patches extending over cheeks and jaws, converging on the chin, but leaving nose and ears unaffected. On the central part of the left cheek is a dollar-sized patch of closely crowded, almost coalescent, peculiarly angular and flattened vesicles, with clear contents, resembling drops of dew. In the labiomental furrow and extending upward to midpoint of lower lip is an intensely erythematous and slightly puffy area with a central group of small, closely set, angular vesicles. There is no glandular enlargement. The eyelids are not affected.

The dorsum of the left hand is puffed up with an elastic, cushion-like swelling, extending to the ulnar border, over the dorsal and lateral surfaces of fingers, and slightly to the palmar surface of the fingers. The swelling prevents closing of hand. A ring on the third finger is almost hidden in the fold of edema. On the dorsum and lateral surface of ring finger are three tensely filled bullæ with rounded summits and clear contents. Two bullæ are each 1 inch long and ⅝ inch wide; the third is round, ¾ inch in diameter. On the dorsum of the middle finger is one bleb, ¾ inch by ⅝ inch. There are no vesicles on hand or other fingers.

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Primrose dermatitis, chronic type, infiltrated and scaling dermatitis.

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The dorsum of the right hand shows a pale, elastic swelling, extending over dorsum of fingers, without erythema, vesiculation, or bleb formation. The palms of both hands are unaffected, but perspire excessively.

On both forearms, more on extensor than on flexor surface, and extending upward to within two inches of elbow, is a blotchy, unevenly distributed, rose-red erythema with irregular margins, with intervening areas of normal skin. The eruption on the two arms is of equal intensity, and erythematous throughout. The remainder of the body is not involved. There is intense itching and burning, especially on lateral surface of fingers.

In other instances the reaction may be of an abortive papulo-vesicular type on an erythematous base, or simply erythematous or urticarial in character, though the latter has been very infrequent in my experience.

The cases which might be termed chronic, owing to repeated attacks at short intervals, present an appearance of acute exacerbation of an infiltrated and scaling dermatitis. On the face the skin is thickened and thrown into folds, especially about the eyes, yellow-red in color and covered with closely adherent, thin scales. Vesiculation during acute attacks is imperfect and small denuded areas, slightly edematous, exude thin serum which dries into gummy, yellow crusts. The active inflammatory process appears as though focused in limited areas, without outlying reaction, and as if it were superimposed, giving an appearance of artificiality to the clinical picture, which is often quite striking.

An analysis of the cases as to age, sex, occupation, and the like, is not only of interest, but reveals some points of value in diagnosis. As the dermatitis results from direct contact with the plant it naturally follows that florists, gardeners, housewives and servants are most prominent in the list of those affected; that females are more often affected than males, and that children almost never develop the dermatitis. I observed several cases among the members of a religious sisterhood, and in merchants who made a hobby of cultivating flowering plants.

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OCCURRENCE

The primula is hothouse-grown and its growth is forced for its sale during the holiday seasons of Christmas and Easter, though it is in the market at all times. Consequently the great majority of cases developed immediately after Easter, following the introduction of the primula into the home as a floral decoration. Others referred the beginning of the dermatitis to the period immediately following a birthday anniversary, at which time the primula had been received as a gift. In the case described earlier, the patient had been presented with a flowering primula at Easter-time for five successive years, and had promptly each time developed a dermatitis, which became increasingly severe with each recurrence. Many exacerbations followed at irregular intervals for several months, and finally the entire process ceased (after the withered plant had been removed), to reappear at the following Easter. Only once was this sequence broken, owing to the presentation of a primula on the patient's birthday and the consequent development of the dermatitis during her stay at a sanatorium, where she had gone to recuperate after several months of suffering from what was regarded as a "nervous eczema."

In another instance the dermatitis made its appearance regularly for three years on Easter Sunday afternoon, had then persisted for weeks, was considered a "gouty eczema" and was each time cured by a stay at a German health resort.

In many instances the history of regularity or periodicity of attacks or exacerbations provides the clue for determining the cause of an otherwise unexplainable dermatitis, and probably nowhere more so than in the primula dermatitis. This is well shown in the history of several cases which I have observed. One patient repeatedly developed the dermatitis shortly after every return to her own home after a period of time spent in visiting friends or traveling; her return after even a few days of

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absence was followed by the outbreak of a dermatitis, her first care always having been the trimming of her plants, including the primula. In another instance a dermatitis of only moderate degree and extent appeared on every successive Sunday and subsided by Thursday or Friday of the same week. This sequence is explained by the regularity with which the primula was trimmed every Friday.

The eruption is most often found on the hands, forearms, and face, including the ears, and in all of the cases observed by me these were the only parts of the body affected. I have been informed of the case of a florist in whom the erythemato-vesicular inflammation extended to the shoulders, with marked swelling of both arms.

It appears that the inflammatory reaction remains limited to those parts which come directly into contact with the plant or to which the irritating principle is transferred. Thus, in one of my cases the ears were intensely affected because of transference from the hands owing to the patient's habit of pulling at the lobes of the ears. In the case of a housemaid the fingers and wrists were the only parts affected, owing to their contact with the primulas contained in a window-box when raising or lowering the window shades. A unique case has been reported by Kirk[6] in which an intense swelling of the oral and pharyngeal mucous membrane resulted from chewing a leaf of the primula.

This limitation of the eruption is in marked contrast to that seen in ivy poisoning, in which areas of the skin remote from the points of original contact are frequently and severely affected.

The first symptoms usually observed are intense burning and itching, without visible change in the skin, which, however, soon responds with an erythematous blush and some swelling. I have not observed a papu-

6. Lancet, 1899, ii, 579, 1630.

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lar eruption, though papulo-vesicles may develop later. Rarely the reaction is entirely of an urticarial nature; that is, an acute edema with serous exudate, sufficient at times to prevent closing of the hand. Small vesicles, closely grouped, develop early, and I have been impressed with the frequency with which the vesicles are angular in outline, as contrasted with the rounded vesicular lesions of eczema. The lateral surfaces of the fingers, dorsum of the hands, and the chin and cheeks show the vesicular eruption most often. In the cases I have seen the palms have always remained normal.

The subsequent course of the eruption may be acute, with the formation of blebs and considerable edema, or more subacute with rapid drying of the vesicles and scaling. The duration of a single attack may be as short as four to five days or may be extended to two weeks before recovery is complete. Acute exacerbations due to renewed exposure may prolong the affection indefinitely, and result in the production of a chronic, infiltrative type of dermatitis, lasting perhaps for several months. Fortunately, however, the discovery of the cause of the dermatitis, or the death of the plant, and consequent absence of further opportunity for renewed infection, allows recovery to take place. In this connection it is interesting to note that although under favorable conditions the primula blooms about every six weeks, it usually, after two or three months of household care, loses its vitality and is discarded, at which time the dermatitis also terminates.

The sleeplessness, anorexia, and general nervous irritability observed in some cases can be fully accounted for by the intense burning and itching which is a prominent feature of even mild types of the dermatitis. Fever, chills, joint pains, and other evidences of constitutional disturbance have never been observed by me, though transient slight rises in temperature are mentioned by Nestler.

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The variation in the degree of reaction exhibited by different persons to the irritating principle contained in the primula, and the apparent immunity of others, is suggestive of the existence of an idiosyncrasy. The study of a large number of cases, however, shows in many a constantly increasing susceptibility, so that even the slightest contact with the toxic agent will eventually result in the production of an intense dermatitis. Others, apparently entirely immune, will later, after repeated exposure, develop an intense reaction just as do those who exhibit an "idiosyncrasy" primarily. Among florists and their assistants this gradual change from immunity to susceptibility is not uncommon, and I have had occasion to observe several such instances. The personal experience of Nestler,[7] detailed in his admirable monograph, in which his immunity was finally succeeded by an intense susceptibility, provides the experimental proof for the assertion that probably no one is entirely immune.

This extremely sensitized state of the skin, causing marked reaction to even minimal amounts of the irritant, is highly suggestive of the development of an anaphylactic condition, and is comparable to the phenomena resulting after repeated introduction of essentially non-toxic sera of a different species. This view is supported by the analogous condition of increased susceptibility of the skin after repeated exposure to the dust of satinwood, with the development of a dermatitis, observed in satinwood workers by Wechselmann.[8] He also calls attention to the fact that in animal experiments parts of the phenomena of anaphylaxis occur in the skin: intense itching, hyperalgesia and spasm of the arrectores pilorum.

Individuals differ in their rapidity of response to the action of the irritant within wide limits. It has been experimentally determined (Nestler) that the dermatitis

7. Hautreizende Primeln, Berlin, 1904.
8. Deutsch. med. Wchnschr., 1909, No. 32.

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may not develop until fourteen days after contact with the plant, although the usual period is from a few hours to two or three days. After repeated attacks the response is more prompt, usually within a few hours following contact. The occasionally prolonged incubation period, and the fact that the primula dermatitis does not always appear after the first contact with the poison, but may require repeated exposures for its development, largely increase the difficulty of diagnosis.

BOTANICAL AND CHEMICAL CHARACTERS

Of the many species of the primrose family only four (*Primula obconica, P. sinensis, P. cortusoides and P. sieboldii*) are known to be capable of producing a dermatitis, according to Nestler's researches, and of these the *Primula obconica* is most virulent and the most frequent offender. *Primula sinensis*, the Chinese primrose, though capable of exciting an intense dermatitis, is less often in question, and will merely be mentioned here.

The *Primula obconica* was introduced into Europe from China in 1883 and several years later began to be extensively cultivated by American florists. The flowers are arranged in a whorl, borne on a slender, cylindrical, hairy stalk, and are pale lilac, pink or purplish in color. The leaves are soft, large, radical, ovate-cordate, hairy, and spring from the root. The leaf-stalk, flower-stalk and midrib are abundantly provided with coarse, easily visible hairs and innumerable fine hairs, the latter being found also on the calyx and corolla. The hairs are all glandular and exude a greenish-yellow material which forms brownish-yellow masses that are readily detached by the slightest touch.

The secretion, including the crystals, is readily soluble in alcohol, ether, chloroform, hydrochloric acid and sulphuric acid, but is insoluble in water (Nestler). Under the microscope the formation of monoclinic crystals can be observed.

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Practically all who have written on the subject of primula dermatitis ascribe its production to an assumed mechanical irritation by the hairs of the plant, because these are pointed and said to be easily detached. My study of the subject, however, led to the conclusion that inasmuch as the hairs are not readily detached and are too soft and supple to act as mechanical irritants, the source of the dermatitis must be sought for in the secretion of the plant. The leaves have a faint aromatic odor, distinct from the perfume of the flower, and this suggests the presence of a volatile oil with toxic properties. Experiments with the secretion applied to my skin were negative except for a temporary tingling and prickling sensation, but produced a mild reaction in a patient who had formerly experienced the dermatitis. Similar results followed the application of the dried residue left after washing a number of leaves with ether. At this time I became acquainted with the experimental work of Nestler on this subject, as detailed in his exhaustive monograph, and have been able to confirm a number of his observations. He was the first to demonstrate the existence of needle-shaped crystals and large and small rhombic prisms in the secretion exuding from and covering the glandular hairs of the leaves. By direct experiment on himself and others he was able to produce a dermatitis with crystals obtained by sublimation of the residue left after flooding the leaves with ether; he thus provides the evidence that in these crystals resides the irritating principle of the primula. Although I have repeatedly found extremely minute needle-like crystals and small rhombic forms in the ether washings and in the untreated secretion of fresh leaves, the larger rhombic formations, as described by Nestler, have thus far escaped my observation. The chemical composition of the toxic principle, however, still awaits solution. Nestler showed further that not alone the fresh leaves, but also the thoroughly dried leaves, contain the irritating substance, which explains the infection occurring

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particularly in housewives, who, when trimming the primula, pick off the dried leaves.

The dermatitis may develop without direct contact with the plant, owing to transference of the secretion to various objects and then to the skin. Nestler was infected several times through the medium of gloves which had been worn while experimenting with the secretion of the plant. In the case of a highly susceptible florist's assistant observed by me the dermatitis developed after handling the paper in which primulas had been packed during shipment. This mode of infection, however, is probably very infrequent, as is also the transmission of infective material from one person to another, as briefly mentioned by Nestler, and direct contact with the plant will be found to have occurred in the great majority of cases.

TREATMENT

Consequently the removal of the primula and thorough cleansing with alcohol of objects which have been in contact with the plant are required to prevent a recurrence of the dermatitis. Alcohol, ether and chloroform are solvents of the secretion, and when applied immediately after contact with the plant have been found by Nestler to prevent the development of the reaction. From my own experience I can confirm this observation, and also Nestler's statement, based on experiment, that alcohol applied immediately on the appearance of the dermatitis, in case there has been a short incubation period, results in a modified and mild course of the inflammation.

In other respects treatment is to be conducted according to the usual principles followed in cases of acute dermatitis. The intense itching and burning are usually promptly relieved on the application of calamin lotion or zinc gelatin, and under a bland ointment the inflammation rapidly subsides and the skin returns to normal after slight desquamation. This rapid subsid-

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ence of an apparently intense inflammatory process of eczematous character, under indifferent treatment, ought to be sufficient to arouse suspicion of the artificial nature of its production and lead to a thorough inquiry as to its external origin.

As a preventive measure it appears desirable for florists to acquaint prospective purchasers of the *Primula obconica* and *Primula sinensis* with the irritating properties of these plants, and thus to assist in not only decreasing the number of cases of dermatitis but in arriving at a correct and early recognition of their cause.

128 Wisconsin Street.

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ALOPECIA AND SEBORRHEA

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Dandruff and loss of hair are two of the minor afflictions of civilized life which are usually sources of constant chagrin to the unfortunate men and women who fall victims to their presence. One or both of these conditions, which even we ourselves experience sooner or later, are brought to our attention as dermatologists so frequently that it seems fitting from time to time to present them as themes for discussion when we meet in the hope that some member here may contribute some small bit of knowledge to a subject which needs so much help from an etiologic and therapeutic standpoint. It is, therefore, because we practitioners are usually so helpless when confronted by a well-established case of alopecia or of seborrhea that I have ventured to summarize my knowledge of these conditions gleaned from the study of 794 examples observed in my personal private practice.

In the following pages I shall deal principally with seborrhea capitis and with alopecia simplex and alopecia furfuracea, but I shall speak superficially on alopecia areata, and alopecia from ringworm, syphilis and overexposure to *x*-rays.

ALOPECIA

Statistically, I record 679 cases of loss of hair divided clinically as follows:

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	Cases	Males	Females
Alopecia simplex[1]	115	37	78
Alopecia furfuracea	443	206	237
Alopecia areata	86	46	40
Alopecia from ringworm	16	9	7
Alopecia from syphilis	17	11	6
Alopecia from *x*-rays	2	1	1
	679	310	369

1. By this term is meant the simple loss of hair without other objective symptoms.

From these figures it will be seen that women are more often affected by loss of hair than men, in the relative proportion of 54 and 46, unless it be that women feel this loss more keenly and therefore consult physicians more freely on this account. It is interesting, however, to note the figures of Elliott,[2] who in his paper of 1892 records about identical percentages, viz. 55 per cent. women and 44 per cent. men. Jackson,[3] on the other hand, in 1893 found the proportions reversed and recorded alopecia in 52 per cent. males and 48 per cent. females.

Possible Etiologic Factors in Alopecia Simplex and Alopecia Furfuracea

From a study of my records it will be noted that heredity, dandruff, systemic depression, fever, operations and maltreatment of the scalp have been connected in the patients' minds with the production of the fall of the hair. Under the heading of systemic depression figure overwork, worry, nervous exhaustion and prostration, recent immigration or foreign travel, pregnancies, and chronic diseases or invalidism. The term "maltreatment of the scalp" is based on my own personal theories as to what is right and what is wrong in the hygiene of the scalp and includes the rough usage of brushes, combs and massage in the presence of dandruff; shampoos less often than once a month or more frequently than once a week; the use of any drugs in

2. Elliot, G. T.: Sixteenth Annual Meeting of Am. Derm. Assn.; see report, p. 81.

3. Jackson, G. T.: Loss of Hair, a Clinical Study Formed in 300 Private Cases, Tr. Am. Dermat. Assn., 1900, p. 50.

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any form on the healthy hair or scalp; the continued application of too drying alkaline soaps; the frequent or constant exposure of the uncovered head to the summer sun; the daily sousing of the head in shower-baths or in salt water; and the modern over-treatment of the normal scalp by barbers and hairdressers.

Statistically we find these factors summed up as follows:

	Cases
Heredity: Father's side of the house	108
Mother's side of the house	51
Not recorded	12
	171
Alopecia present in brothers or sisters	72

From these figures it is seen that a hereditary taint exists in 30 per cent. of these individuals. Dandruff was present in 443 patients, a percentage of 79+. Systemic depression was recorded in 120 cases, a percentage of 21+. Fever was noted in 63 individuals, a percentage of 11+. Operations were blamed in 12 persons, a percentage of 2+. Maltreatment was evident in 277 patients, a percentage of nearly 50; and, finally, more than one of the above possible etiologic factors was found in 386 cases, a percentage of approximately 70.

It may be interesting to pause a moment and compare these figures with those of Dr. G. T. Elliot[4] and of Dr. G. T. Jackson[3] who based their figures on 344 and 300 cases respectively.

	Heredity	Systemic Causes	Seborrhea
Elliot	1.16*	5.52	91.68
Jackson	38.32	.....	72.66
C. J. White	30.64	21.50	79.39

* This percentage relates to alopecia simplex only.

The figures which follow in the rest of this paper are not wholly satisfactory and are comparatively small, as the symptoms had existed so long in many cases that patients were unable to remember the exact date of their beginnings.

4. Elliot, G. T.: Alopecia and Its Most Frequent Cause, Dermatitis Seborrheica, Tr. Am. Dermat. Assn., 1895, p. 95.

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Ages When Alopecia Simplex First Appeared

Among those who could be exact there were 25 males and 43 females out of a possible 37 and 78 respectively.

Males: 7 cases began between 16 and 20.
8 cases began between 21 and 25.
6 cases began between 26 and 30.
1 case began at 35.
1 case began at 39.
2 cases began at 46.

It will be seen that this clinically uncomplicated type of loss of hair begins at or before the age of 30 in 84 per cent. of the male cases.

Females: 7 cases began at or before the age of 15.
3 cases began between 16 and 20.
5 cases began between 21 and 25.
4 cases began between 26 and 30.
7 cases began between 31 and 35.
2 cases began between 36 and 40.
6 cases began between 41 and 45.
6 cases began between 46 and 50.
2 cases began between 51 and 55.
1 case began at or before the age of 56.

Of the seven early cases five followed acute febrile disturbances. Between the ages of 15 and 30, however, we find that 33 per cent. of these women developed their simple alopecia, contrasted with a respective percentage of 84 in men, whereas between the ages of 31 and 50 we note a percentage of 58, figures which force us to the conclusion that alopecia simplex develops much later in women than in men.

Ages When Dandruff and Alopecia Appeared in Alopecia Furfuracea

DANDRUFF

Males, 91 cases.
3 cases began between 9 and 10
8 cases began between 11 and 15
31 cases began between 16 and 20
25 cases began between 21 and 25
14 cases began between 26 and 30
8 cases began between 31 and 35
1 case began at 37 and 1 at 43

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Females, 75 cases.

3	cases	began	between	7	and 10
12	cases	began	between	11	and 15
10	cases	began	between	16	and 20
13	cases	began	between	21	and 25
11	cases	began	between	26	and 30
12	cases	began	between	31	and 35
7	cases	began	between	36	and 40
3	cases	began	between	42	and 45
4	cases	began	between	46	and 56

Contrasting these two columns of statistics we are struck by two facts, viz., that men are more prone to remember the exact date when their dandruff began than is the case with women and that in these men and women seborrhea capitis appeared at an earlier period in the former sex than in the latter. Thus between the years 16 and 25 we find 61 per cent. of males developing their dandruff while in females at a similar epoch we find but 32 per cent.

ALOPECIA

Males, 127 cases.

6	cases	began	between	10	and 15
30	cases	began	between	16	and 20
55	cases	began	between	21	and 25
14	cases	began	between	26	and 30
14	cases	began	between	31	and 35
2	cases	began	between	36	and 40
3	cases	began	between	41	and 45
2	cases	began	between	46	and 50
1	case	began	at	60	

Females, 129 cases.

7	cases	began	between	12	and 15
24	cases	began	between	16	and 20
21	cases	began	between	21	and 25
25	cases	began	between	26	and 30
25	cases	began	between	31	and 35
16	cases	began	between	36	and 40
5	cases	began	between	41	and 45
1	each	at	46, 51, 54, 61, 63	and	68

In these columns it is seen that men and women are apparently equally impressed by the exact age at which their hair begins to fall but that between the ages of 16 and 25 alopecia develops in 67 per cent. of the men affected against 34 per cent. in the women.

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Thus from these foregoing contrasting figures we learn that men are attacked much earlier than the opposite sex by alopecia furfuracea whereas women as a whole become the victims of alopecia, either simple or furfuraceous, more often than men, in fact, in the proportion of 56 to 43

Varieties, Distribution, and Subjective Symptoms of Dandruff and Loss of Hair in Alopecia Furfuracea

DANDRUFF	Cases.	ALOPECIA	Cases.
Slight in	127	Slight in	67
Abundant in	199	Marked in	130
Localized in	83	General in	30
Yellow-brown in	56	Principally on forehead in	119
Oily in	78	Principally on top of head in	79
Dry in	53	Principally on sides in	13
Granular in	23	Principally at tonsure in	38
Adherent in	38	Hair dry in	37
Loose and large in	39	Hair greasy in	15
Accompanied by pruritus in	97	Hair split in	49
Accompanied by burning in	3	Hair short in	34
Accompanied by hyperidrosis in	30	Hair coarse in	8
		Hair fine in	21

These figures require no elucidation. It is evident from their study that in alopecia furfuracea we may expect to encounter more often well-marked examples of seborrhea and of loss of hair than the reverse; that dandruff is usually general in distribution, while alopecia is generally localized; that dandruff is frequently accompanied by subjective symptoms and is often associated very strikingly with many changes in the texture of the hair as well as in its loss.

The Treatment of Alopecia Furfuracea

I fear that we must all agree that our therapeutic results in this disease are very disheartening. I tell all my patients who have noted this condition for more than a few months, and especially those whose forebears have been similarly affected, that a permanent

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cure is hardly to be hoped for, but that by long and continued perseverance on their part they may keep their scalps clean and delay the inevitable baldness for years.

The medical aphorism which tells us that therapeutic non-success may be judged by the multiplicity of the drugs recommended in a given disease is well emphasized in the present instance.

My armamentarium has included the following medicaments:

Washes, containing 70 per cent. alcohol, quinin, cantharides, capsicum, pilocarpin, chloralhydrate, tartaric and salicylic acids, phenol, formaldehyd, trikresol, anthrasol, and croton and turpentine oils.

Ointments, containing sulphur, salicylic acid, zinc oxid, resorcin, oil of cade, ichthyol, succus limonis, yellow oxid and ammoniated chlorid of mercury, orthoform and biborate of soda.

Soaps, containing betanaphthol and glycerin.

Internal medication, including iron, nux vomica, magnesium sulphate, dilute sulphuric acid, betanaphthol, malt, cod-liver oil, phenyl salicylate, ichthyol, salicin, thyroid extract and phosphate of soda.

Massage:

Despite this long list I practically confine myself to four prescriptions which I append:

1. ℞.	gm. or c.c.	
Acid salicyl		
Sulph. precip. āā	2	or 3ss
Petrolatum	32	ʒi

M. S.—Ointment. Apply at night. Shampoo with a simple soap the following day.

2. ℞.	gm. or c.c.	
Pilocarpin nitrat.	.06	gr. i
Quinin sulph.	6	or gr. x
Tr. canthar.		
Tr. capsic. āā	10	3iii
Alcohol, 70 per cent. ad	250	fl. ʒviii

M. S.—Wash for scalp. Apply in the morning.

3. ℞.	gm. or c.c.	
Acid tannic	2	26 gr. xxxv
Chloral hydrate	1	66 gr. xxvii
Acid tartaric	2	gr. xxx
Ol. ricini	1	or m. xv
Alcohol, 70 per cent.	200	fl. ʒvi

M. S.—Wash for scalp. Apply in the morning.

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4. ℞.	gm. or c.c		
Hydrarg. chlorid. corrosiv.....		24	gr. iv
Euresol	8	or	ʒii
Sp. formicarum	30		ʒi
Ol. ricini	4-12		ʒi-iii
Alcohol, 70 per cent. ad.....	250		ʒviii

M. S.—Wash for scalp (poison). Apply two teaspoonsful in the morning.

The last of these four I hold easily first in its successful results. I associate its formula with Dr. G. T. Elliot, and it has proved a veritable godsend to me in treating many of these almost impossible cases. The essential feature in its composition is, I believe, euresol —the mono-acetate of resorcin. The smell of this salt is a very unfortunate factor, however, but one which the manufacturers have not been able to eradicate without markedly diminishing the value of the drug. The chloral hydrate wash I place second in efficacy.

Perhaps the most striking feature of these four prescriptions seems to be the absence of pure resorcin from their composition. I am free to confess that I never have been able to reduce its strength sufficiently to render it anything but an irritant to the scalp.

Results of Treatment Summarized by Age

These figures are comparatively small because many patients came but once and hence cannot be included in these lists.

MALES, 200 CASES

Very good, 16 cases

At 19 2 cases
Between 20 and 25, 4 cases
Between 26 and 30, 3 cases
At 31 1 case
Between 41 and 45, 3 cases
Between 46 and 50, 2 cases
At 58 1 case

Slight, 58 cases

Between 15 and 20, 10 cases
Between 21 and 25, 20 cases
Between 26 and 30, 13 cases
Between 31 and 35, 6 cases
Between 36 and 40, 2 cases
Between 41 and 50, 4 cases
Between 53 and 63, 3 cases

Bad, 9 cases

Between 20 and 26, 4 cases
At 32 2 cases
At 38, 42 and 53, 1 case

Good, 80 cases

At 13 and 14, 2 cases
Between 16 and 20, 10 cases
Between 21 and 25, 16 cases
Between 26 and 30, 23 cases
Between 31 and 35, 13 cases
Between 36 and 40, 9 cases
Between 41 and 45, 3 cases
At 49, 56, 65 and 75, 1 case

Poor, 37 cases

At 18 and 19, 2 cases
Between 21 and 25, 14 cases
Between 26 and 30, 8 cases
Between 31 and 35, 7 cases
Between 36 and 40, 4 cases
Between 42 and 46, 2 cases

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FEMALES, 194 CASES

Very good, 17 cases		Good, 93 cases	
At 13	1 case	Between 11 and 14,	4 cases
Between 26 and 30,	4 cases	Between 16 and 20,	7 cases
Between 31 and 35,	5 cases	Between 21 and 25,	19 cases
At 38	2 cases	Between 26 and 30,	15 cases
Between 47 and 50,	3 cases	Between 31 and 35,	16 cases
Between 56 and 60,	2 cases	Between 36 and 40,	12 cases
		Between 41 and 45,	7 cases
		Between 46 and 50,	4 cases
		Between 51 and 55,	3 cases
		Between 57 and 60,	3 cases
		At 63, 80, 83 each,	1 case
Slight, 53 cases		Poor, 25 cases	
Between 5 and 9,	2 cases	Between 11 and 15,	2 cases
Between 13 and 15,	4 cases	Between 16 and 20,	2 cases
Between 16 and 20,	2 cases	Between 21 and 25,	3 cases
Between 21 and 25,	11 cases	Between 26 and 30,	6 cases
Between 26 and 30,	11 cases	Between 31 and 35,	4 cases
Between 31 and 35,	7 cases	Between 36 and 40,	2 cases
Between 36 and 40,	4 cases	At 50, 56, 60	2 cases
Between 41 and 45,	3 cases		
Between 46 and 50,	5 cases		
Between 51 and 55,	2 cases		
At 70	2 cases		
Bad, 6 cases			
At 15	1 case		
Between 30 and 37,	2 cases		
Between 43 and 48,	3 cases		

From these figures it is seen that the prognosis in women is better than in men in the proportion of 56 per cent. to 48 per cent. These percentages are based on the "very good" and the "good" results in both sexes; and in addition we see that there were fewer "poor" and "bad" results in women than in the men in the proportion of 16 per cent. to 23 per cent. Therefore, we may encourage our feminine patients decidedly more than we can our masculine.

SEBORRHEA

Included in this study of 794 cases were found 117 individuals who were the subjects of dandruff alone. It is rather a disconcerting fact to find so many examples of seborrhea capitis without resulting loss of hair, especially as this condition had existed for many years in many of these people—disconcerting because in this

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paper it has been inferred, at least, that dandruff is the most frequent cause of alopecia. Nevertheless, when the data are put into cold figures it will be found that these inferences are perhaps not wholly wrong. In the list there are 115 cases of alopecia simplex or a total number of 232 individuals in whom dandruff has played no part in the production of loss of hair. On the other hand there is a total of 443 men, women, and children, a ratio of nearly two to one, in whom dandruff and loss of hair were present and in whom, by the figures in the great majority of instances, the seborrhea had preceded the alopecia for varying lengths of time.

To return to our cases of seborrhea simplex. Of the 117 examples 54 were males and 63 females, a ratio of 46 to 54—a distinct feminine preponderance and curiously enough corresponding absolutely exactly to our percentages of alopecia from various causes recorded in the early part of this communication (see above).

Age When Seborrhea Began

Males, 32 cases		Females, 29 cases	
At 1, 11, 14 each,	1 case	At 1, 7 each,	1 case
Between 16 and 20,	8 cases	Between 10 and 15,	7 cases
Between 21 and 25,	2 cases	Between 16 and 20,	10 cases
Between 26 and 30,	10 cases	Between 21 and 25,	5 cases
Between 36 and 40,	4 cases	Between 26 and 30,	4 cases
Between 53 and 60,	4 cases	At 41	1 case
At 65	1 case		

These are rather small figures from which to draw conclusions but one is struck by the fact that dandruff comes on in childhood or in early adult life—71 per cent. in men and 96 per cent. in women exhibiting this symptom at or before the age of 30.

Incidence of Seborrheic Symptoms Other Than Dandruff

For some years it has been my custom to regard seborrhea as merely the cutaneous evidence of some internal disorder and to look on acne vulgaris, acne rosacea, eczema seborrheicum and Fordyce's disease of the lips as similar expressions of the same general disturb-

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ance. So, from a study of these records, I find that in the 443 cases of alopecia furfuracea there were 57 individuals (a percentage of 12, consisting of 31 males, and 20 females) who exhibited one or more of these allied eruptions; while in the 117 examples of seborrhea simplex there were 29 men and 38 women (a total of 67, or a percentage of 57) with similar efflorescences.

DYSPEPSIA

As to the nature of the fundamental disorder which, some think, lies at the bottom of these seborrheic symptoms we are decidedly at sea. Many of us, however, are wont to accuse digestive disturbances as possible sources of trouble and in this series of cases clinical evidences of dyspepsia have been found in the following percentages: in alopecia simplex 3; in alopecia furfuracea 8; and in seborrhea simplex 17. Surely, these are small crumbs of comfort to the believers in the digestive origin of these disorders.

Regions Affected in Alopecia Areata and in Ringworm

ALOPECIA AREATA, 86 CASES

Scalp, 71 cases		Ringworm, 9 cases	
Occipital,	36 cases = 50 %	Occiput,	5 cases = 55 %
Parietal,	11 cases = 15 %	Top of head,	2 cases = 22 %
Top of head,	8 cases = 11 %	Sides,	1 case = 11 %
Frontal,	5 cases = 7 %	Beard,	1 case = 11 %
General,	11 cases = 15 %		

Face, 21 cases	
Beard,	13 cases = 62 %
Upper lip,	5 cases = 24 %
Eyebrows,	3 cases = 14 %

No comment is necessary on these figures; they are very small but they speak for themselves. In scrutinizing my cases of alopecia areata I was struck by the marked incidence of an accompanying dandruff. This statement of course coincides with Sabouraud's dictum that pathologically and bacteriologically seborrhea always precedes or accompanies alopecia areata. Another fact impressed on my mind in the study of these cases is that one attack of alopecia areata very often leads to one or more successive outbreaks.

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SUMMARY

This then brings me to the end of these numerous columns of figures and deductions, which in conculsion I may summarize as follows:

1. Alopecia accompanied by dandruff is the commonest type of loss of hair.

2. Women are more prone to alopecia than men, in the proportion of 54 to 46.

3. The possible and principal causal factors of alopecia are heredity in 30 per cent., dandruff in 79 per cent., systemic depression in 20 per cent, fever in 11 per cent., and maltreatment of the scalp in 50 per cent.

4. Alopecia simplex develops before the age of 30 in 84 per cent. of the men, but in only 33 per cent. of the women.

5. Dandruff behaves in a similar manner and before the age of 25 attacks 61 per cent. of its future male victims but only 32 per cent. of its female.

6. The loss of hair in alopecia furfuracea comports itself with these previous two findings, appearing before the age of 25 in 67 per cent. of the men, but only in 34 per cent. of the women.

7. Summarizing paragraphs 2, 4, 5, and 6, we find that men are attacked earlier than women with alopecia and with seborrhea but that eventually women rather than men fall victims to these conditions.

8. When dandruff is present it is apt to be abundant rather than slight, oily rather than dry, and to be accompanied by itching.

9. With alopecia we find well-marked cases rather than mild ones, located in the great majority of the cases in the frontal and temporal regions and accompanied by hair which is apt to be dry, split, short and fine.

10. The drugs most successful in the treatment of dandruff and loss of hair are euresol, bichlorid of mercury, tannic acid and chloral hydrate.

11. The final results of treatment in these affections are almost disheartening, but judged from a temporary

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point of view, we may expect good or very good response in 48 per cent. of men and in 56 per cent. of women.

12. Seborrhea may exist for years without entailing any appreciable loss of hair; nevertheless, dandruff does seem to be followed or accompanied by alopecia twice as often as not.

13. Seborrhea simplex is a disease of childhood or early adult life, developing before the age of 30 in 71 per cent. of men and 96 per cent. of women.

14. Other seborrheas of the skin such as acne vulgaris, acne rosacea, eczema seborrheicum and Fordyce's disease, may accompany loss of hair and dandruff. Their percentages of concomitance, however, vary, and consist of 12 per cent. in alopecia furfuracea and 57 per cent. in seborrhea simplex.

15. Dyspepsia, on the other hand, exists in surprisingly small percentages in these cases, being present in only 3 per cent. in alopecia simplex, 8 per cent. in alopecia furfuracea, and 17 per cent. in seborrhea simplex.

16. From the preceding two paragraphs we may induce that seborrhea simplex is a truer form of dandruff than that accompanying loss of hair.

17. In alopecia areata and in ringworm of the scalp, the region most affected is the occipital.

18. In alopecia areata dandruff is a frequent accompaniment and we also find that one attack of the disease is apt to be followed by one or more later outbreaks.

259 Marlborough Street.

ABSTRACT OF DISCUSSION

DR. WILLIAM O. ROOP, Dayton: I indorse Dr. White's statement in regard to the value of euresol in treatment of these diseases of the scalp. I have frequently included it in my application in the treatment of these seborrheic conditions, and it has given me better results than some of the older remedies.

I have been consulted during the past year in several cases of alopecia areata, and in all I was particularly struck

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by the accompanying seborrhea; and while the recognized treatment has always been of a stimulating character, I felt that inasmuch as the etiology of alopecia areata is somewhat in dispute, that perhaps the same treatment as for seborrhea, and of a less stimulating character than that usually employed, might be successful. With that idea in view, I used a simple ointment of sulphur and resorcin, rubbing it into the patches at night, and in a number of instances I have been rewarded by a rapid return of hair in these bald areas. In other cases I have used treatment of a more stimulating character, such as applications of chrysarobin, phenol and the high-frequency current, but I was surprised to observe that my results were more rapid and satisfactory from use of the milder methods. This would suggest that alopecia areata may be of seborrheic origin since the two affections are so frequently concurrent and both yield to the same treatment.

Dr. Frank C. Knowles, Philadelphia: In anticipation that Dr. White would dwell on the subject of alopecia areata, I have reveiwed the dispensary reports of four hospitals, the Pennsylvania, University of Pennsylvania, Howard, and Children's, with which I am connected. During the last five years I have seen 105 cases of this disease, twelve of this number being of the universal type. Alopecia areata of dental origin has recently been reported by several writers; Jacquet has written most extensively on this phase of the subject. Rousseau-Decelle (*Bull. et mém. de la Soc. méd. des hôp.*, 1909, p. 62) has described several cases. Jourdanet (*Bull. de la Soc. francaise de dermat. et de syph.*, April, 1910), detailed an alopecia areata of the nape of his own neck following caries of a wisdom tooth. Traumatism seemed to have been etiologic in a few of my cases. In my collection of photographs are five pictures of a case of universal alopecia, in a boy of sixteen. The various stages and relapses of the disease, extending over a period of three and one-half years, are plainly shown. The last photograph, which was taken in May, 1910, shows complete restoration of all the hair.

Dr. J. M. King, Nashville: Dr. Whitfield, of King's College, London, who has the reputation of being a very careful and competent observer, has found some defect of vision in nearly all his patients with alopecia areata. I remember that whenever such a patient consulted him, he always had the vision tested. In treatment, the prescription that I have used, in alopecia of the seborrheal type has been made up of bichlorid of mercury, resorcin, chloral hydrate, tincture of cantharides, glacial acetic acid and alcohol. I first saw this used in St. George's Hospital, London, and I found that it acted very well indeed in a number of cases. I have not tried euresol, as this mixture has served me well in con-

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junction with sulphur ointment, used once every week or two weeks, the night before the application of green soap shampoo.

DR. ALFRED SCHALEK, Omaha: I was surprised to hear that seborrhea was an incurable disease, as my experience has not borne that out. I believe that it is curable in the majority of cases if the treatment is sufficiently prolonged. In one case of alopecia areata in which I applied the high-frequency current, the coincident seborrhea of a severe type from which the patient was also suffering largely disappeared, and from that time on I have used the high-frequency current in these cases with good results.

DR. J. B. KESSLER, Iowa City: The statement made by Dr. White that alopecia was more common in females than in males rather took me by surprise. My experience has been the reverse. In the hospital with which I am connected there are about 45 nurses in the training-school; after they have been in the hospital six or eight months many of them complain that they are losing their hair. Last summer, in connection with some of my colleagues, I took up this matter to see if the cause of this loss of hair could be determined. We investigated the cooking and the quality and quantity of the food, which was up to the average and sufficiently nourishing, and the only possible etiologic factor we could find was a lack of exercise in the open air. These nurses were on continuous duty for twelve hours and then returned to the Nurses' Home to sleep and study. It seems to me that this is the most prolific cause of alopecia in this class of people. I believe that women, as a rule, take better care of their hair than men, and when the hair becomes affected they are apt to follow the physician's directions more faithfully than men.

I have had some experience with euresol, and while it is very efficient, it is also very expensive, $1.00 an ounce making the price almost prohibitive. I have found, usually, in these forms of alopecia, that ointments are better in the beginning than solutions, and that the latter are more effective when they are preceded by the use of ointments. A favorite application of mine—although its odor is objectionable—is the oil of cade and sulphur. I first learned the value of this mixture while I was in Boston, working under the elder Dr. White. Euresol was brought to my attention through the kindness of Dr. Charles J. White; my results with this remedy, as well as those of my son, have been very satisfactory. I keep up the application for about a month, when the dandruff can be easily removed and the scalp will remain free from it for a reasonable length of time. There are some cases, however, and I have one under my observation at the present time, in which all methods of treatment are more or less unsatisfactory.

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DR. ISADORE DYER, New Orleans: I want to sound one note in the danger of the use of the hair brush. I have preached for many years that no patient with dandruff will recover until the hair brush is discarded. There are only two ways of sterilizing it: One is by boiling and the second is by burning it. In the propagation of dandruff, the barber-shop is probably the chief offender, and I believe that an inspection of the usual ancient hair brush found in the wash-room of the country hotel or in any public place will demonstrate the destruction of the bristles of the brush itself by the micro-organism. The men who are interested in the work of this Section, as well as all dermatologists, should carry on this crusade against the hair brush as I have long done in my own city. I have frequently seen patients in whom the recurrence of dandruff invariably followed a visit to the barber shop. While on a visit aboard, after I had been free from dandruff for many years, I visited a barber shop and warned the barber not to use the brush. Just as he was completing his work, however, he forgot my instructions and gave one stroke with the hair brush. Five days later I again began to treat my scalp for dandruff. I cannot concede that the particular form of seborrhea which we call dandruff is incurable. I instruct male patients to wash their scalp every day; the female patients every other day, or at least twice a week. An experience extending over a number of year, has justified my faith in the use of resorcin, 2 to 5 per cent. solutions. Euresol has no advantage over this, in my own experience. In fair-haired patients, or those who have hair tinged with gray, the resorcin must be modified or some substitute employed. By neglecting this precaution, I have once or twice in my early experience inflicted on my patients hair which in color resembled the plumage of a canary bird. Chloral hydrate serves in these cases: it is an excellent stimulant to the scalp and an efficient antiseptic. I have never seen a case of alopecia areata which I believed to be parasitic, or in which I was not able to demonstrate a neurotic basis. I remember one case in which these bald patches recured for nearly a year; the patient's occupation was that of a driver of a fire engine, and when he gave that up, his hair promptly and permanently returned.

In the treatment of this condition, I regard the high-frequency current as more satisfactory than any other.

DR. M. L. HEIDINGSFELD, Cincinnati: The basis of our present treatment of alopecia rests on the experiements of Lassar and Bishop, which were carried on 30 to 40 years ago on mice, rabbits and other animals. For fifteen or 20 years the results of this work were unquestioned: when they were controverted by Blaschko, who maintained that alopecia was not a parasitic condition. Blaschko carried out a series of experiments similar to those of Lassar and Bishop, and his results

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were absolutely negative. Treatment of this condition at the present time is based largely on the theory that it is of parasitic origin. Personally, I concur in the belief that premature baldness is not a parasitic condition. I think that too much manipulation of the scalp by rubbing and massaging is injurious both in men and in women. Premature baldness is accompanied by four cardinal symptoms, i. e., itching, dandruff, a dry or oily condition of the scalp, and, lastly, loss of hair. Dandruff is only a precursor of the loss of hair, and in order to prevent the occurrence of the latter, we must control the itching, the dandruff and the abnormal condition of the scalp. Treatment must be directed against these special conditions. Resorcin, if too strong or too frequently applied, will produce an oily condition of the scalp. An oily scalp may be rendered less oily, or even dry, by substituting colloidal sulphur or nascent sulphur, after the formula of Radcliffe Crocker for the resorcin.

Dr. William Frick, Kansas City: In the alopecia accompanying syphilis the loss of hair is not always limited to the scalp. I recently saw a case in which the alopecia of the scalp was not complete, but there was a complete loss of the eyebrows and eyelashes.

Dr. William A. Pusey, Chicago: One factor in regard to alopecia has not been mentioned and is worthy of consideration, particularly with the present fashion, and that is, excessive exposure of the scalp to sunlight. We are all familiar with the middle-aged man riding horseback or playing golf bareheaded in the forlorn hope of bringing his hair back. For many years I have regarded this excessive exposure to sunlight as an exciting factor in the production of alopecia. I have noticed that many of these patients apply for treatment in the autumn, after they had gone bareheaded throughout the summer, and I was also led to this idea through the analogy of the effect of the sun's rays with those of the x-rays. We know that with highly actinic energy we can produce baldness, and I am inclined to believe that free exposure to sunlight will have the same effect. This is probably only one of many factors, and in my opinion alopecia is a condition of complicated etiology; it is not a well-grounded view that all alopecias or nearly all are parasitic.

I have never been able to convince myself of the value of many of the remedies that have been mentioned in the treatment of this condition. This is true of resorcin, with which I have had a very unsatisfactory personal experience. I know of only two remedies that have a definite value in the treatment of alopecia, namely, tar and sulphur. I have used alcohol in various combinations, and it is my impression that about as much good is accomplished by alcohol alone as when it is combined with other remedies.

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DR. J. GRINDON, St. Louis: It is a popular notion that frequent washing injures the scalp, but practically, I have observed that those who are the most inveterate and constant in the practice of washing the scalp keep their hair as long as anybody else, and I always tell my patients that they can wash their heads as often as they please. Nor can I understand how the application of soap and water to the surface of the scalp can have any bad effect on the growth of the hair. In regard to medication in these cases, I have had very good results from the use of resorcin, and I agree with Dr. Kessler that solutions are usually more effective when they are preceded by the use of ointments. One of my favorite prescriptions is composed of petrolatum, salicylic acid and sulphur. I tell my patients that this application is disagreeable, but that it will probably not be necessary to continue it for longer than a month. After this I use resorcin, usually a 2 per cent. solution, either alone or in combination. In cases of well-established seborrheal alopecia I tell my patients that I do not believe that I shall ever be able to give them an actual permanent cure, but that I hope to bring about a symptomatic cure, providing they keep up the treatment indefinitely. As long as they live they will be obliged to pay some attention to the scalp in order to avoid a recurrence. So far as the effect on the scalp of exposure to the rays of the sun is concerned, I must agree with Dr. Pusey on theoretical grounds. The comparative frequency with which cases of loss of hair are observed in the autumn I attribute not to the effect of the sun's rays, but rather to the fact that there is natural loss of hair at that period of the year, whether one plays golf bareheaded or not. The α-ray, in small doses, causes a growth of hair, while large doses produce a loss, and the actinic rays from the sun in such doses as we get them, probably stimulate the growth of hair. Our ancestors, who wore no clothing at all, had hair all over their bodies.

DR. J. B. KESSLER, Iowa City: I have in mind a case of universal alopecia in a boy of 18 in whom the condition has now lasted about 2 years. With the exception of two or three little stubs, his body and scalp are completely bare. He has beeen examined by a neurologist and his blood has been examined with entirely negative results. I have been unable to find the cause of the alopecia or a remedy for it.

DR. FRANCES ROWLEY, Galveston: Has anyone studied this matter with reference to the diet of the patient? Has the nitrogenous metabolism been investigated, or would these patients receive any benefit by increasing the sulphur?

DR. C. J. WHITE, Boston: The diversity of opinions expressed well illustrates the fact that we really do not know anything about this subject scientifically. We have our pet

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theories, and we reason largely by analogy. I agree with Dr. Pusey in regard to the effect on the hair of over-exposure to sunlight. I believe that the scalp and hair are supposed to have a certain amount of grease, and if we expose the scalp to the sun, we remove the greasy element and the hair becomes bleached. For the same reason, constant washing of the head or over-treatment of the scalp is equally disadvantageous. This history of too much sun or too much washing I have frequently obtained from persons who were prematurely bald.

My colleagues and I in Boston have never derived much benefit from the use of resorcin in this disease. If it is applied strong enough to do any good, it inflames the scalp. As to a possible deficiency of sulphur in the economy, to which Dr. Rowley referred, I do not know whether any scientific work has been done in that direction, but I have given that drug internally in one of its several forms without resulting benefit.

I tell my patients to use a hair brush as little as possible unless it is a clean one, and instruct them to sterilize it by placing it in the sun for a few hours at least once a week. I agree with Dr. Dyer that the hair brush is a very common cause of the persistence of dandruff. In treatment in general, I have tried all the various ointments, and in my hands they did not work so well as the two lotions that I have described. I believe that women are affected with alopecia oftener than men, but there are cases in which men feel more keenly than women the loss of their hair. As to the various etiologic factors of alopecia areata referred to by Dr. Knowles, I do not think we know the true cause of the affection, but I believe that in some specific organism plus the stimulus of a nervous breakdown or sudden shock or the debilitating effect of slow sepsis from carious teeth we have a reasonable theory of the origin of this disease.

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RECENT PROGRESS IN THE SERUM DIAGNOSIS OF SYPHILIS

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In reviewing the literature on the serum diagnosis of syphilis that has appeared since the last meeting of this Association, I have attempted to call attention to the progress that has been made during the year rather than to discuss at length the present status of our knowledge of the subject. The continued interest in the Wassermann reaction, and in various other serodiagnostic tests for syphilis, is shown by the large number of serious researches and clinical reports that have appeared during the past year. Four excellent books on the subject have been published in German, English and French. It was proper that the first of these should have been written by one of the discoverers of the Wassermann reaction, Carl Bruck,[1] whose personal experience with the test has been enormous. He has given a most excellent presentation of the whole subject from both the theoretical and practical standpoints. Noguchi[2] has also written a book of great value, in which special attention is devoted to his own modification. Interesting booklets have also been published by Gastou and Girauld[3] in France, and by Mulzer[4] in Germany.

1. Bruck, C.: Die Serodiagnose der Syphilis, Julius Springer, Berlin, 1909.
2. Noguchi, H.: Serum Diagnosis of Syphilis, and the Butyric Acid Test for Syphilis, J. B. Lippincott, New York, 1909.
3. Gastou, P., and Girauld, A.: Guide pratique du diagnostic de la syphilis, J. B. Baillière et Fils, Paris, 1910.
4. Mulzer, P.: Praktische Anleitung zur Syphilisdiagnose auf biologischem Wege, Julius Springer, Berlin, 1910.

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VARIOUS SERODIAGNOSTIC TESTS

Before discussing the more important subject of the Wassermann reaction I should like to call attention to some of the serodiagnostic tests for syphilis, depending on principles other than those of complement-fixation. I had supposed that the status of the various precipitation tests for syphilis was fairly well settled at the last meeting of this association. In a paper read on that occasion Wieder and L'Engle,[5] from experiments with sodium taurocholate and glycocholate, lecithin, taurin and water, concluded that the proportion of positive results in non-syphilitics was too high to make the test of value. This seemed to be the prevailing opinion last year and is, I think, at present, in spite of two recent reports on the subject. Rosenfeld and Tannhauser,[6] in a series of 131 cases, obtained results that compared favorably with those of the Wassermann test. Tanton and Combe,[7] from an examination of sixteen cases, concluded that the precipitation method was equally specific, in addition to being much simpler than the Wassermann reaction. Sourd and Pagniez,[8] however, found that the precipitation test gave six positive reactions in non-syphilitic cases, and Paris and Sabaréanu,[9] from an examination of fifty-three cases, conclude that the test is of no diagnostic value whatever. A similar opinion is expressed by Laub and Novotny[10] in regard to the value of the reaction for pathologic-anatomic diagnosis, their

5. Wieder, H. S., and L'Engle, E. M.: Some Studies of the Precipitation Test for Syphilis, THE JOURNAL A. M. A., Nov. 6, 1909, p. 1535.

6. Rosenfeld, F., and Tannhauser: Die Serodiagnose der Lues mittels Ausflockung durch glykocholsaures Natrium, Deutsch. med. Wchnschr., 1910, xxxvi, 165.

7. Tanton and Combe, E.: Le séro-diagnostic de la syphilis par la méthode de Porges, Compt. rend. Soc. de biol., 1910, lxviii, 436.

8. Le Sourd, L., and Pagniez, P.: La réaction précipitante du sérum syphilitique vis-à-vis des solutions de glycocholate de soude, Compt. rend. Soc. de biol., 1909, lxvii, 84.

9. Paris, A., and Sabaréanu: La séro-précipitation chez les syphilitiques par le glycocholate de soude, Compt. rend. Soc. de biol., 1910, lxviii, 290.

10. Laub, M., and Novotny, J.: Ueber die Brauchbarkeit der Porgesschen Ausflockungsreaktion fur die Diagnose der Lues an Leichen, Ztsch. f. Immunitätsforsch., 1909, iii, 394.

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experiments including a simultaneous test of ninety-eight cadaver serums. Unfavorable results are also reported by Minelli and Gavazzeni.[11] In all of the above communications the test with glycocholate of soda was the one employed.

Since the publication of Noguchi and Moore[12] last July on the butyric acid test in the metasyphilitic and nervous diseases, nothing further has been written on this method. In their experiments the writers found that the test was not absolutely specific, positive reactions having been obtained in two out of thirty-seven psychoses not in any way related to syphilis. In his book on serum diagnosis Noguchi states that the butyric acid test while not entirely specific, is at times more valuable than the Wassermann reaction in excluding syphilis, for instance, when the reaction is negative.

Assuming that the modus operandi of the Wassermann reaction depends on a precipitation, Jacobsthal[13] suggests a method which he terms the "optic serodiagnosis of syphilis." The patient's serum is mixed with alcoholic extract of syphilitic liver in the proportion of 1 to 10 and the resulting precipitate is examined with the dark-field illuminator. A strong positive reaction appears as a clumpy precipitate, a weak positive reaction as a small conglomeration of little fat particles, while a negative is shown as a thick emulsion of very fine dancing fat particles. In comparing his method with the Wassermann reaction Jacobsthal claims that, after having acquired the necessary experience, his results with the two tests were identical.

It can hardly be of more than historical interest to discuss the color reaction suggested by Schürmann,[14]

11. Minelli, S., and Gavazzeni, G. A.: Il metodo di Porges nella sierodiagnosi della sifilide, Gazz. med. ital., 1909, lx, 191.
12. Noguchi, H., and Moore, J. W.: The Butyric Acid Test for Syphilis in the Diagnosis of Metasyphilitic and Other Nervous Diseases, Jour. Exper. Med., 1909, xi, 605.
13. Jacobsthal, E.: Die optische Serodiagnose der Syphilis, München. med. Wchnschr., 1909, lvi, 2607.
14. Schürmann, W.: Luesnachweis durch Farbenreaktion, Deutsch. med. Wchnschr., 1909, xxxv, 616.

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that has been so thoroughly discredited by subsequent experimentation. Indeed, it seems strange that so much has been written on the subject when it seemed almost from the start that the method was valueless. A few words about this proposed method may aid in preventing others from further experimentation. Schürmann thought that there might possibly be some substance in the blood of syphilitics whose presence could be recognized by a color reaction. It occurred to him that lactic acid might play a part in the reaction, as this substance had been present in one of his most reliable extracts. His first experience with Uffelmann's reagent being unsuccessful, he was led to use perhydrol in combination with phenol and chlorid of iron. According to Schürmann, when the reagents were mixed with normal serum a light green color appeared at the upper portion of the mixture. This either disappeared or changed to a light green tint on shaking, the solution remaining clear. When syphilitic serum was used a blackish-brown dull tint appeared almost immediately, the solution giving the impression of a thick mixture.

Employing his method in eighty-four cases simultaneously with the Wassermann test, Schürmann claimed to have obtained identical results. In a comparison of the Schürmann with the Wassermann test in 154 cases of undoubted syphilis Meirowsky[15] obtained 62.3 per cent. of positive reactions for the Wassermann test as opposed to 14.9 per cent. for the Schürmann method. The list of investigators whose results have been unfavorable, and who conclude that the test is of no clinical value, includes Biach,[16] Bonola,[17] Braunstein,[18]

15. Meirowsky, E.: Die Schürmannsche Methode des Luesnachweises mittels Farbenreaktion, Deutsch. med. Wchnschr., 1909, xxxv, 937.

16. Biach, M.: Ueber Luesnachweis durch Farbenreaktion, Wien. klin. Wchnschr., 1909, xxii, 606.

17. Bonola, F.: Sulla reazione cromatica di Schürmann per la sierodiagnosi della sifilide, Riforma med., 1909, xxv, 682.

18. Braunstein, A.: Ueber die Schürmannsche Farbenreaktion bei Lues, Ztschr. f. klin. med., 1909, lxviii, 345.

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Bruck,[1] Galambos,[19] Roth and Goldner,[20] Schminke and Stoeber,[21] C. Stern,[22] Stühmer,[23] Symanski, Hirschbruch and Gardiewski.[24] According to the chemical examination of Braunstein,[18] the reaction is a process of oxidation, the perhydrol oxidizing the phenol by means of the iron chlorid.

Interesting results have been obtained by Nicolas, Favre and Gautier[25] with dermic and intradermic reactions in syphilis, analogous to the reaction caused by tuberculin for the diagnosis of tuberculosis. For this purpose the experimenters used a concentrated glycerinated extract of liver of syphilitic fetus which they termed "syphiline." When this extract was used by the dermic method (as in the von Pirquet test), no change was noted. When, however, the extract was injected intradermically a reaction consisting of redness and nodular infiltration was obtained in a large proportion of the twelve cases examined. In a second contribution the same authors[26] give the results in fifty cases, of a comparison of their test with the Wassermann reaction. The results were in agreement in forty-two cases. Of the remaining eight cases five seemed to favor the correctness of the diagnosis by the intradermic test, while one favored the Wassermann method.

The relation of the Wassermann test to the antitryptic power of the blood in syphilis was studied by Fuersten-

19. Galambos, A.: Ueber den Wert der Farbenreaktion bei Lues, Deutsch. med. Wchnschr., 1909, xxxv, 976.

20. Roth, A., and Goldner, V.: Ueber die Farbenreaktion bei Lues, Orvosi hetil., 1909, No. 19. (Review in Monatsh. f. prakt. Dermat., 1909, l, 129.)

21. Schminke and Stoeber: Zur Kritik der Schürmannschen Farbenreaktion bei Lues, Deutsch. med. Wchnschr., 1909, xxxv, 937.

22. Stern, C.: Ueber die Bewertung einer Serum-Farbenreaktion zum Luesnachweis, Berl. klin. Wchnschr., 1909, xlvi, 1068.

23. Stühmer, A.: Luesnachweis durch Farbenreaktion, Fortsch. d. Med., 1909, xxvii, 714.

24. Symanski, Hirschbruch and Gardiewski: Luesnachweis durch Farbenreaktion, Berl. klin. Wchnschr., 1909, xlvi, 874.

25. Nicolas, J., Favre, M., and Gautier, C.: Intradermoréaction et cutiréaction avec la syphiline chez les syphilitiques, Compt. rend. Soc. de biol., 1910, lxviii, 257.

26. Nicolas, J., Favre, M., and Charlet, L.: Comparaison des résultats fournis par l'intradermo-réaction à la syphiline et par la séro-réaction de Wassermann, Bull. et mém. Soc. méd. d. hôp. de Paris, 1910, xxvii, 440.

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berg and Trebing.[27] The determination of the antitryptic index (using a modified method of Müller and Jochman) was made simultaneously with the Wassermann method in sixty-one cases of syphilis and other diseases. It was found that in cases of undoubted syphilis giving a positive reaction the antitryptic titer or index was never increased. In the majority of cases it was diminished. Whether this test will prove of value, from the fact that an increased antitryptic titer would seem to exclude syphilis, can be judged only after further investigation with this method.

According to Achard, Benard and Gagneux,[28] the so-called leukodiagnosis, which is based on specific sensitiveness of leukocytes *in vitro* to certain normal or pathologic products, may also be applied to syphilis. The specific principle used by these writers was a glycerinated extract of spleen of a congenitally syphilitic infant containing *Spirochæta pallida*. The strongest influence on the leukocytes was obtained with a 5 per cent. dilution of the extract. In this strength the leukocytic activity was found to be more or less increased in syphilis, while it was not at all influenced in healthy subjects. It was found in their investigations that the strongest reactions correspond to the period of early secondary syphilis, while the reactions were weaker in hereditary manifestations of the disease and in tabes and paresis.

The reaction first described by Much and Holzmann was tried by Hamburger[29] in twenty-two cases of syphilis simultaneously with the Wassermann test. The results obtained were entirely contradictory, the writer concluding that the test has no value in syphilis. The reaction which has previously been seen only in certain insane

27. Fuerstenberg, A., and Trebing, J.: Die Luesreaktion in ihren Beziehungen zur antitryptischen Kraft des menschlichen Blutes, Berl. klin. Wchnschr., 1909, xlvi, 1357.

28. Achard, C., Benard, H., and Gagneux, C.: Leuco-Diagnostic de la Syphilis, Compt. rend. Soc. de biol., 1910, lxviii, 323.

29. Hamburger, J.: Ueber die Beeinflussung der Kobra-Gift-Hämolyse durch Seren von Haut- und Geschlechtkrankheiten, Dermat. Ztschr., 1909, xvi, 785.

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persons, especially dementia præcox, consists in an inhibitory action to the hemolysing power of cobra venom.

In experimenting with various hemolysing agents in different diseases it was found by Richard Weil[80] that the erythrocytes of syphilitics were especially resistant to the hemolysing power of cobra venom. This fact has been utilized as the basis of a diagnostic test for syphilis that promises to be of considerable value. The technic of the procedure is as follows: Blood is drawn into a 2 per cent. solution of sodium citrate, washed and made into a 4 per cent. suspension in normal salt solution. It is then tested on the following day. Equal amounts of venom at 1 to 800 and 1 to 1,500 are added and after one hour of incubation the results are read. It has been found that syphilitic cells resist a solution of 1 to 1,800; that is, twice as strong as that which destroys the control. The reaction was found to be marked in 90 per cent. of the cases of syphilis, the percentage of positive reactions being smaller in tabes than in paresis. In several non-syphilitic affections in which the Wassermann test was positive (three cases of scarlatina, two cases of polycythemia and one case of scleroderma) the Weil test showed a negative reaction. Some advantages which Weil claims for his test are that it can be used in cases of jaundice. It is positive for some time after mercurial treatment has abolished the Wassermann reaction. It is finally positive in a very large percentage of old quiescent cases in which the Wassermann test is negative. Dr. Weil informs me in a personal communication that he considers his test too delicate for general use, as a very considerable amount of practice is required in order to interpret the results obtained.

80. Weil, R.: The Resistance of Human Erythrocytes to Cobra Venom., Jour. Infect. Dis., 1909, vi, 688; The Variation in the Resistance of Human Erythrocytes in Disease to Hemolysins, with Especial Reference to Syphilis, Proc. Soc. Exper. Biol. and Med. 1910, vii, 2.

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The meiostagmin reaction suggested by Ascoli and used by him as a diagnostic procedure in typhoid fever has been applied by Izar[31] to syphilis. The test is a physico-chemical reaction of immunity depending on a change in surface tension of the fluids employed. When the serum of a syphilitic is mixed with its corresponding antigen and placed in the thermostat for two hours there is a diminution in surface tension as shown by an increase in the number of drops of a measured amount of the fluids. According to Izar the test was found to be entirely specific. A positive reaction was obtained in twelve cases of syphilis, while all of the non-syphilitic cases gave negative results, including two cases of leprosy in which the Wassermann reaction had been positive.

WASSERMANN TEST AND ITS MODIFICATIONS

In reviewing the recent progress of the Wassermann reaction I should first like to discuss some of the more important and practical contributions that relate to the technic of the method. A simple means of obtaining the patient's blood for examination has been suggested by Muck.[32] The superficial veins of the neck are compressed by Bier's method and the mucous membrane of the anterior portion of the septum is scratched with a small needle or knife. In about three minutes as much as 20 c.c. of blood can be readily secured. The bleeding stops on removal of the compression, or on introduction of a pledget of cotton into the nose. Another method of obtaining blood where a venepuncture is difficult or not desirable, as in infants, is suggested by Somani.[33] After

31. Izar, G.: Ueber eine spezifische Eigenschaft luetischer Blutsera, München. med. Wchnschr., 1910, lvii, 182.

32. Muck, O.: Die Schleimhaut der Nasenscheidewand eine besonders geeignete Stelle für die Blutentnahme zu der Wassermannschen Reaktion und zu anderen serologischen Untersuchungszwecken, München. med. Wchnschr., 1909, lvi, 2321.

33. Somani, B. P.: Quantitative Bestimmung der luetischen Serumveränderung mittels der Reaktion von Wassermann, Neisser und Bruck, Arch. f. Dermat. u. Syph., 1909, xcviii, 73.

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scarifying the skin he applies a cupping apparatus with an outlet below attached to a test-tube to receive the blood, and a suction-pump attached in the center. To this and other cupping methods Mulzer makes the objection that the apparatus is difficult to sterilize and that unsightly scars are left which if the method were widely adopted and known to the laity might at times prove compromising.

Finkelstein[34] has devised an apparatus for determining quantitatively the strength of a positive reaction. He uses a glass funnel (of a shape to fit a centrifuge), at the bottom of which a graduated tube is fused. The undissolved corpuscles of the case to be examined and of the known positive cases are poured into two separate funnels, which are then centrifugalized and the result mathematicaly read. A somewhat similar apparatus has been recently suggested by Heimann.[35]

As yet no one has produced the much-desired artificial antigen which shall prove as reliable and specific as the various organ extracts now in use. The artificial antigen of Sachs and Rondoni has, however, been found in the hands of Eisenberg and Nitsch[36] to be the equal of organ extracts, while unfavorable results in its use were obtained by Isabolinsky.[37] An artificial antigen has been suggested by Schürmann[38] which, in addition to lecithin, contains glycerophosphate of sodium and ammonium vanadinate. This has been tested by Rajchman and Zygmunt[39] with disappointing results. They conclude

34. Finkelstein, J. A.: Zur Technik der Wassermannschen Reaktion, Berl. klin. Wchnschr., 1909, xlvi, 1611.

35. Heimann, W. J.: A Method for the Mathematical Reading of the Original Wassermann Reaction, THE JOURNAL A. M. A., May 21, 1910, p. 1684.

36. Eisenberg, R., and Nitsch, R.: Ueber Wassermannsche Reaktion mit künstlicher Antigen, Przeglad. Lekarski, 1909, No. 32. (Reviewed in Monatsh. f. prakt. Dermat., 1909, l, 131.)

37. Isabolinsky, M.: Weitere Untersuchungen zur Theorie und Praxis der Serodiagnostik bei Syphilis, Ztschr. f. Immunitätsforsch., 1909, iii, 143.

38. Schürmann, W.: Ein künstlicher Extrakt zur Anstellung der Luesreaktion, Med. Klin., 1909, v, 627.

39. Rajchman, L., and Zygmunt, S.: Praktische Bemerkungen zu der Frage der Wassermannschen Reaktion, Przeglad. Lekarski, 1909, No. 25. (Reviewed in Monatsh. f. prakt. Dermat., 1909, l, 138.)

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that artificially prepared antigens are not reliable substitutes for alcoholic organ extracts, as in weak doses they often fail to give positive reactions with syphilitic serums and in stronger doses give a positive reaction with normal serums.

It was recently pointed out by Wechselmann[40] that the failure to obtain higher percentages by positive reactions in cases of undoubted syphilis might be due to interference from the presence of complementoids. By removing these disturbing bodies, by shaking the serum with barium sulphate, better results were obtained than with the regular Wassermann method. This procedure has been tried by Lange[41] with strikingly good results in a series of 800 cases, in which both methods were simultaneously performed. In 551 syphilitic serums the Wechselmann test yielded 85 per cent. of positive reactions, as against 77 per cent. for the Wassermann method. In non-syphilitic control cases the Wechselmann test gave only negative reactions. Shaking the serum with barium sulphate not only adds to the delicacy of the test, but also destroys the complement, making it unnecessary to inactivate the patient's serum by heating to 56 C. for a half hour. Lange, therefore, at the present time uses the barium sulphate treatment of the serum as a substitute for inactivation by heat.

In order that positive and negative control serums may always be at hand Hecht[42] recommended that they be preserved by means of drying. Small amounts, such as 0.5 c.c., are dried in watch crystals. When the serum is needed it is dissolved in an equal amount of salt solution, after which equal amounts of distilled water are added. The combination of salt solution and water is advised, as when distilled water is added to the dried

40. Wechselmann: Ueber Verschleierung der Wassermannschen Reaktion durch Komplementoidverstopfung, Ztschr. f. Immunitätsforsch., 1909, iii, 525.

41. Lange, C.: Ergebnisse der Wassermannschen Reaktion bei Vorbehandlung der Sera mit Baryumsulfat nach Wechselmann, Deutsch. med. Wchnschr., 1910, xxxv, 217.

42. Hecht, H.: Zur Technik der Seroreaktion bei Syphilis, Ztschr. f. Immunitätsforsch., 1910, v, 572.

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serum certain substances (possibly globulins) remain undissolved and float about in the mixture as cloudy masses.

According to Blanck and Friedmann[43] alcoholic extracts of syphilitic liver at times lose their usefulness for the Wassermann reaction by being kept in the ice-chest or in a cold solution. They found that in some cases this could be remedied by allowing the extract to remain in a thermostat for several days. To preserve their efficiency best it is advised to keep extracts in a warm room.

Further researches on the feasibility of using urine in place of serum for the Wassermann reaction have been made by Pollio.[44] His conclusions are similar to those of Höhne, that the use of the urine has no practical value, as too large a percentage of positive reactions are given in non-syphilitic cases. Even Blumenthal and Wile, who first experimented with urine, admitted that it was not quite as reliable as blood-serum for the Wassermann test. Bauer and Hirsch[45] conclude that in positive reactions obtained by using urine the inhibition of hemolysis is due to the globulin fraction of the urine. They obtained negative results in non-syphilitic urine containing albumin and in syphilitic urine containing no albumin, or albumin in small amounts.

In a discussion by Stern[46] of uncertain and paradoxic reactions that are so often obtained by every serologist, some of the rules are given that are at present followed in the laboratory of the Neisser clinic at Breslau. Every serum is tested both by the original Wassermann and by the Stern method; that is, in both active and inactive

43. Blanck and Friedmann: Ueber thermoreversible Zustandsänderungen der bei der Wassermannschen Reaktion verwendete alkoholischen Leberextrakte, Ztschr. f. Immunitätsforsch, 1909, iii, 108.

44. Pollio, G.: La reazione di Wassermann eseguita colle urine ha valore pratico, Riforma med., xxv, 231.

45. Bauer, R., and Hirsch, A.: Beitrag zum Wesen der Wassermannschen Reaktion, Wien klin. Wchnschr., 1910, xxiii, 6.

46. Stern, M.: Ueber die Bewertung der unsicheren und "paradoxen" Reaktion bei der serodiagnostichen Untersuchung der Syphilis, Ztschr. f. Immunitätsforsch., 1910, v, 201.

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condition. When the results are not in accord the serums of the cases that are clinically doubtful are tested once or more times, using various extracts known to be reliable. The same procedure is followed in serums giving a partial inhibition of hemolysis and in serums of apparently healthy persons giving a positive reaction.

That the Wassermann reaction as originally performed is not absolutely satisfactory from either the theoretical or practical standpoint is apparent from the many attempts that have been made to improve and simplify the test. Of the different methods depending on the principle of complement-fixation there are eight which might be termed systems, which were published before June, 1909. The principles on which these different systems are constructed are very plainly shown in a comparative table by Noguchi in his book on serum diagnosis.

Since last June another "system" has been added to the list by Foix,[47] who suggests the use of rabbit's blood for the indicator in place of sheep's blood. During the past year the modifications[48] of Bauer, Tschernogubow (second method), and more especially those of Hecht and Stern, have been the subject of a good deal of investigation in Europe, while the method of Noguchi has received especial attention in America. The final word is yet to be pronounced on these various modifications, as there is not yet an absolute opinion as to their value.

47. Foix, C. H.: Sur une technique simplifiée de réaction de fixation, Compt. rend. Soc. de biol., 1909, lxvii, 171.

48. The modification of Bauer dispenses with immune (artificial) amboceptor and depends on the natural antisheep amboceptor present in the patient's serum. The Hecht method dispenses not only with the immune amboceptor but also with the guinea-pig complement, utilizing the complement normally present in the patient's serum. Stern in her modification also relies on human complement, but unlike Hecht uses the immune amboceptor. Tschernogubow in his second method employs the red corpuscles of the guinea-pig instead of the sheep as his indicator. He also makes use of human complement. Noguchi employs human corpuscles as the indicator, guinea-pig serum for complement, and antihuman amboceptor.

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Very favorable results with the Hecht test are reported by König,[49] who finds it superior to both the original method and that of Margarete Stern. In a more recent communication on the method of Hecht, the same writer[50] concludes that it fulfils all the requirements of any modification, which are that: 1. It must have a scientific basis. 2. It must be simpler and more delicate than the original method. 3. It should never give erroneous results. Demanche and Ménard[51] conclude that the results of the Hecht test are practically as reliable as those of the original method. Scholtz[52] speaks of the test as simple and reliable. From his experience with 500 cases performed simultaneously with the Wassermann test, Werther[53] considers the Hecht method preferable, as it gives less often an incomplete inhibition; e. g., doubtful results. Favorable expressions of opinion on this method are also given by Stanculéanu and Liebreich[54] and by Sabrazes and Eckenstein.[55] Unsatisfactory results with the Hecht and with the Bauer test are reported by Hügel and Reute,[56] while both of these methods, as well as those of Stern and Tschernogubow, are condemned by Isabolinsky as giving less certain results than the Wassermann test.

49. König: Warum ist die Hechtsche Modifikation der Wassermannschen Luesreaktion dieser und der Sternschen Modifikation vorzuziehen? Wien. klin. Wchnschr., 1909, xxii, 1127.

50. König: Ueber die Hechtsche Modifikation der Wassermannschen Seroreaktion, Deutsch. med. Wchnschr., 1910, xxxvi, 506.

51. Demanche, R., and Ménard, P. J.: Valeur de la méthode de Hecht pour le séro-diagnostic de la syphilis; comparison avec la réaction de Wassermann, Compt. rend. Soc. de biol., 1910, lxviii, 714.

52. Scholtz, W.: Ueber die jetzige Bedeutung der Wassermann Neisserschen Reaktion für die Diagnose und Therapie der Syphilis, Klin.-therap. Wchnschr., 1909, xvi, 1190.

53. Werther: Ueber das Wesen und den Wert der Wassermannschen Reaktion und 500 eigene Untersuchungen mit der Hechtschen Modifikation, Monatsh. f. prakt. Dermat., 1910, l, 147.

54. Stanculéanu, G., and Liebreich, N. E.: Die Anwendung der Methode von Bauer-Hecht für die Serumdiagnose bei Augenerkrankungen, Revista stüntzelor Med., 1909.

55. Sabrazès, J., and Eckenstein, K.: Note on a Simple Method of Fixation of the Complement in Syphilis, Lancet, London, 1910, clxxviii, 233.

56. Hügel and Reute: Bisherige Erfahrungen über die Serodiagnostik der Syphilis an der dermatologischen Universitätsklinik zu Strassburg, München. med. Wchnschr., 1910, lvi, 79.

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The modification of the Hecht test, still further simplified by Fleming by the use of very small amounts of the ingredients, is condemned on the one hand by Bassett-Smith[57] and recommended on the other hand by Clemenger.[58] The former found that hemolysis failed to occur in 30 per cent. of his cases, whereas the latter found only 5 per cent. of failures.

Opinion on the second method proposed by Tschernogubow (the first method having been abandoned) do not seem to entirely agree. Stühmer,[59] from a comparative examination with the Wassermann test in over 300 cases, concludes that the procedure of Tschernogubow represents a great simplification and that its results are at least as reliable as those given by the original method. On the other hand, Guth[60] considers the test unsuited for a large laboratory, as the serum must be used immediately after being obtained, while for practicing physicians its performance is difficult.

In reviewing the results obtained with the Stern modification we again find conflicting reports. An unfavorable opinion is given by Kleinschmidt,[61] who thinks that the use of this procedure may lead to errors in diagnosis. In a comparative examination of 200 cases discrepancies were found to the advantage of the Wassermann method in twenty-five cases. In 5 per cent. of the cases there was not sufficient complement to complete the hemolysis. Jacobeus and Bachmann[62] consider the modification of Bauer and Stern unreliable, as they give too many pos-

57. Bassett-Smith, P. W.: The Diagnosis of Syphilis by Some Laboratory Methods, Brit. Med. Jour., 1909, ii, 377.

58. Clemenger, F. J.: The Diagnosis of Syphilis by Some Laboratory Methods, Brit. Med. Jour., 1909, ii, 575.

59. Stühmer, A.: Ueber die von Tschernogubow angegebene Modifikation der Wassermannschen Reaktion, Deutsch. med. Wchnschr., 1909, xxxv, 1517.

60. Guth, H.: Ueber eine (ii) von Tschernogubow angegebene Modifikation der Wassermannschen Reaktion, Deutsch. med. Wchnschr., 1909, xxxv, 2319.

61. Kleinschmidt, H.: Ueber die Sternsche Modifikation der Wassermannschen Reaktion, Ztschr. f. Immunitätsforsch., 1909, iii, 512.

62. Jacobeus, H. C., and Bachmann, E. L.: Sur les différentes modifications de la réaction de Wassermann, Compt. rend. Soc. de biol., 1909, lxvii, 449.

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itive reactions in non-syphilitic cases. As treated cases of syphilis generally show an increased amount of amboceptor and complement, they suggest that a positive Bauer reaction (depending on natural amboceptor) or a positive Stern (depending on natural complement) might be considered as giving an unfavorable prognosis and indicating prolonged treatment. Schlimpert[63] and Meirowsky[64] warmly recommend the Stern modification, though both of these writers urge that it be performed simultaneously with the original Wassermann method.

NOGUCHI TEST

From this cursory review of the modifications that have been tested with considerable thoroughness abroad it is easy to see that no one method has succeeded in replacing the original procedure of Wassermann. It is unfortunate that the system of Noguchi has not as yet been more seriously considered by our foreign colleagues. In the recent book on serum diagnosis by Gastou and Girauld[3] the method is described at some length, although it has been practically performed only in a few cases. Among those of us in America who have had experience with the Noguchi method there is little doubt as to its very great value. The principles of the test, as well as minute instructions for preparing the reagents, are so plainly described in Noguchi's book that it seems strange that the method has not at least been given a trial in some of the foreign laboratories. In a recent contribution Noguchi[65] has tabulated the work of different American investigators who have experimented with his method, and it may be said that the results speak for themselves.

63. Schlimpert, H.: Beobachtungen bei der Wassermannschen Reaktion, Deutsch. med. Wchnschr., 1909, xxxv, 1368.

64. Meirowsky, E.: Ueber die von M. Stern vorgeschlagene Modifikation der Wassermann-Neisser-Bruckschen Methode, Berl. klin. Wchnschr., 1909, xlvi, 1310.

65. Noguchi, H.: Further Studies on the Serum Diagnosis of Syphilis with Especial Reference to the Antihuman Hemolytic System, Internat. Clin., 1910, Series 20, I, 22.

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The test has now been tried in over 8,500 cases, many of these in comparison with the regular Wassermann test. Kaplan, who formerly reported 8 per cent. positive reactions in non-syphilitic cases, states that during the past five months no such non-specific reactions have occurred. To meet the objections of Swift, who found thirty-five positive reactions in 201 non-syphilitic cases, Noguchi recently gave a public demonstration of his test at the clinic of the Pennsylvania Hospital. The serums of fifty-nine patients were simultaneously examined by Dr. Noguchi with his method, and by Dr. Swift, using the original technic of Wassermann. The results were absolutely identical.

SPECIFICITY OF WASSERMANN REACTION

The question of the specificity of the Wassermann reaction finally appears to be nearing a solution. The list of non-syphilitic diseases in which a positive reaction can be obtained more or less often is becoming more definitely settled. To this list, which includes leprosy, frambesia, sleeping-sickness, scarlatina, and malaria, must now be added, apparently, lupus erythematosus acutus. Fortunately these conditions do not often present any difficulty in being clinically differentiated from syphilis.

Several communications on the Wassermann reaction in leprosy have recently appeared in which the number of patients examined was fairly large. While agreeing that leprosy in general often gives a positive reaction, they do not agree as to the type of the disease in which the reaction is found. Thus Ehlers and Bourret,[66] in forty-seven cases of nodular and anesthetic types, found positive reactions in all except two cases. On the other hand, Eliasberg,[67] in fifty cases, found a much higher

66. Ehlers and Bourret: Wassermann-Reaktion ved Spedalsked. Ugesk. f. Laeger., 1909, No. 49. (Reviewed in Ztschr. f. Immunitätsforsch., 1909, Ref. II, 1007.)

67. Eliasberg, J.: Komplementablenkung bei Lepra mit syphilitischem Antigen, Deutsch. med. Wchnschr., 1909, xxxv, 1922.

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proportion of positive reactions in the nodular than in the anesthetic type. My own results[68] in an examination of sixty patients agree closely with those of Eliasberg, the latter obtaining only three reactions in nineteen anesthetic cases, while I found three reactions in twenty-two cases of this type.

Teissier and Bénard[69] in 100 cases of scarlatina found the reaction partially or completely positive in 84 per cent. of the cases. The reaction appeared at times as early as the third day and invariably disappeared at the end of convalescence. Using extract of human heart as antigen, Nanu-Muscel and Titu[70] obtained only negative reactions in 12 cases of malaria. In 8 cases the examination was made at the height of the paroxysm when the blood showed the presence of the plasmodium. According to Boehm[71] a positive reaction can be obtained in malaria only when the parasites are present in the blood.

In a case of that very rare condition, lupus erythematosus acutus, Reinhart[72] obtained a positive Wassermann reaction on two different occasions. After the patient's death a positive reaction was obtained from the blood. The autopsy showed no evidence whatever of syphilis. A second case of this disease is reported by Hauck,[73] in which on two occasions a positive reaction was found. In this case the patient survived and failed to show the reaction after the acute symptoms had subsided.

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68. Fox, H.: The Wassermann and Noguchi Complement-Fixation Test in Leprosy, Am. Jour. Med. Sc., 1910, cxxxix, 725.

69. Teissier, P., and Bénard, R.: Recherches sur la réaction de Wassermann dans la scarlatine, Compt. rend. Soc. de biol., 1910, lxviii, 272.

70. Nanu-Muscel, J., and Titu, V.: La réaction de Wassermann dans la malaria, Compt. rend. Soc. de biol., 1910, lxviii, 188.

71. Boehm, W.: Malaria und Wassermannsche Reaktion, Malaria, 1909, i, 191.

72. Reinhart, A.: Erfahrungen mit der Wassermann-Neisser-Bruckschen Syphilisreaktion, München. med. Wchnschr., lvi, 2092.

73. Hauck: Positiver Ausfall der Wassermann-Neisser-Bruckschen Syphilisreaktion bei Lupus erythematosus acutus, München. med. Wchnschr., 1910, lvii, 17.

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Interesting results are recorded by Wolfsohn[74] from an examination of 50 patients shortly after ether narcosis. A more or less strong positive reaction was found in 13 cases. Two of these patients were syphilitics, in whom the positive reaction persisted, while in the other cases the reaction disappeared in a few days. Wolfsohn concludes that in 22 per cent. of the cases a temporary positive reaction may be present as a result of ether narcosis. He considers his results as a new proof of the biologic non-specificity of the Wassermann test, and of its close relation to lipoid bodies, as the lipoid substances of the brain and cord are the ones that are bound up in the anesthetic and cause narcosis.

The rather surprising statement is made by Gjorgjevic and Savnik[75] that in examining 24 psoriasis patients giving no history or signs of syphilis, a positive reaction was obtained in 20 cases. As the majority of the reactions were only weakly positive their results will have to be disregarded unless confirmed by other investigators.

Actuated by the report of Bass, who, using lecithin as antigen, found 6 positive reactions in 6 pellagra patients, I examined 30 patients[76] with this disease with the Noguchi modification. My conclusions were that pellagra does not often give a positive reaction. The few reactions obtained were weak and easily distinguished from those found in cases of syphilis. In a discussion of my paper Dr. Bass stated that in subsequent examinations in which he used organ extracts as antigen his results were similar to mine.

To show finally how small after all is the proportion of positive reactions obtained in non-syphilitic cases,

74. Wolfsohn, G.: Ueber Wassermannsche Reaktion und Narkose. Deutsch. med. Wchnschr., 1910, xxxvi, 505.

75. Gjorgjevic, G., and Savnik, P.: Ueber die Wassermannsche Reaktion bei Lues und bei Psoriasis vulgaris, Wien. klin. Wchnschr., 1910, xxiii, 626.

76. Fox, H.: The Wassermann Reaction (Noguchi Modification) in Pellagra, New York Jour., 1909, xc, 1206.

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Bruck has collected from the literature 5,028 control cases in which only 59 positive reactions were found. This seems indeed a small number when the possibility of unrecognized latent infection is considered.

The diagnostic value of a positive Wassermann reaction is now almost universally recognized. This is admitted even by Blanck,[77] one of the severest critics of the test. It may be said in this connection that the most unfavorable criticisms, such as those of Kopp and of Blanck, are usually expressed by men who have had no personal experience in performing the reaction. The question of absorbing interest to the practicing physician as to whether treatment of syphilis can be controlled by means of serum diagnosis, has unfortunately not been settled. It would seem that the problem cannot be solved until we are certain of the significance of a positive reaction. In other words, can it be said that a positive reaction represents the presence somewhere in the body of active syphilitic virus? If this question can be answered affirmatively, it would seem to me that a positive reaction would always indicate antisyphilitic treatment.

In favor of this view Fritz Lesser[78] has advanced the following arguments: 1. There is a parallelism between the number of positive reactions (49 per cent.) that have been obtained in the later stages of latent syphilis, and the number of cases showing post-mortem evidence of syphilis, in whom during life no manifestations of the disease had been present. 2. There is, further, a parallelism between a positive reaction and clinical manifestations. In many cases the reaction changes from positive to negative with the disappearance of lesions and again becomes positive when relapses occur. 3. Under antisyphilitic treatment the reaction changes from positive to negative. In comparing the results of the reac-

77. Blanck: Die Bewerthung der Wassermannschen Reaktion für die Behandlung der Syphilis, Berl. klin. Wchnschr., 1909, xlvi, 1652.
78. Lesser, F.: Die Behandlung der Syphilis im Lichte der neueren Syphilisforschung, Deutsch. med. Wchnschr., 1910, xxxvi, 116.

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tion in cases that had formerly been treated it was found that those that had been thoroughly treated gave a greater number of negative reactions than the ones in whom the treatment had been less thorough.

The significance of a negative reaction from the therapeutic standpoint depends largely on the time that has elapsed since the infection, and since the last injection of mercury. It cannot be judged from the test alone whether we have to deal with latency or with an actual cure of the disease. A negative reaction during the first two or three years seems to be generally considered of small value. If in later years repeated negatives are obtained in a person who shows no clinical manifestations, and who has not recently taken mercury (preferably five months), it would be considered by some that the disease had been cured. It should certainly be looked on as a most favorable result.

FIELD OF APPLICATION OF SERODIAGNOSTIC TEST

The large amount of investigation on the Wassermann reaction during the past year has been productive of some results of very practical value. Much light has been thrown on various questions, such as the problems of syphilitic heredity, prostitution, and the reliability of the test for post-mortem diagnosis. Some valuable contributions relating to the special branches of medicine have also appeared which tend either to prove or to disprove the relationship of certain diseases to syphilis.

Of great importance are the results that have been obtained in diseased conditions of the heart and arteries. Donath[79] concludes that the syphilitic etiology of aortic insufficiency and aneurism, as well as cases of clinically suspicious mesaortitis, is proven by having obtained a positive Wassermann reaction in 85 per cent. of the

79. Donath, K.: Ueber die Wassermannsche Reaktion bei Aortenerkrankungen und die Bedeutung der provokatorischen Quecksilbersbehandlung für die serologische Diagnose der Lues, Berl. klin. Wchnschr., 1909, xlvi, 2015.

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cases. Bruckner and Galesco[80] think that syphilis plays the principal rôle in the etiology of aortic insufficiency, as they found a positive reaction in 17 out of 22 cases. The five patients giving a negative reaction were younger persons, from 14 to 20 years of age, who had suffered from repeated attacks of rheumatism. From an examination of twenty-five cases of various lesions of the heart, Oigaard[81] found positive results in patients suffering from aortic aneurism and uncomplicated aortic insufficiency while negative reactions were obtained in those with lesions of the mitral valve. In 8 out of 9 cases of aortic insufficiency the reaction was also found to be positive by Krefting.[82]

From a study of 130 cases of disease of the eye in which the Noguchi test was performed, Martin Cohen[83] found some interesting results. He considers that "in brain cases with choked discs in which the indications for operations are doubtful and lues is suspected, the presence or absence of the reaction furnishes a valuable confirmatory aid which is speedier or probably more satisfactory than the therapeutic test." He further states that some light may be thrown on the heretofore obscure etiology of retinitis pigmentosa from the large proportion of positive reactions obtained. His conclusion that the Wassermann test is of value in the diagnosis of diseases of the eye is shared by Schumacher[84] and by Hessberg.[85]

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80. Bruckner, J., and Galesco: Syphilis et insuffisance aortique, Compt. rend. Soc. de biol., 1910, lxviii, 74.

81. Øigaard: Wassermann-Reaktionens Betydning ved Hjerte og Karsygdomme, Hosp., Tid., 1909, No. 49. (Reviewed in Ztschr. f. Immunitätsforsch., 1910, ii, 1008.)

82. Krefting, R.: Leichensera und die Wassermannsche Syphilisreaktion, Deutsch. med. Wchnschr., 1910, xxxvi, 366.

83. Cohen, M.: The Value of the Sero-diagnosis of Syphilis in Ophthalmology: A Preliminary Report, Arch. Ophth., 1910, xxxix, 93.

84. Schumacher, G.: Die Serodiagnose der Syphilis in der Augenheilkunde nebst Bemerkungen über die Beziehungen der Tuberculose zur Syphilis bei Augenleiden, Deutsch. med. Wchnschr., 1909, xxxv, 1915.

85. Hessberg, R.: Beiträge zur Bedeutung der Serodiagnose der Syphilis für die Augenheilkunde, Klin. Monatsbl. f. Augenh., 1910, xlviii, Beilageheft, p. 60.

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The application of the Wassermann reaction to otologic cases has apparently added to our knowledge of the cause of nerve-deafness. In examining 29 patients with this condition Busch[86] found 15 strongly positive reactions, or 52 per cent., from which he concludes that syphilis plays a more important rôle in the etiology of nerve-deafness than has previously been supposed. Similarly Beck[87] has found 10 positive reactions in 34 cases of internal ear disease in which there was no disease of the sound-conducting apparatus. In a recent examination (Noguchi test) of 128 cases of ear disease by E. P. Fowler[88] it was found that the greater number of positive reactions in adults were obtained in cases of nerve-deafness and chronic catarrhal disease of the middle ear.

Some opinions regarding the relationship of syphilis to ozena may have to be revised in the light of recent experience with the Wassermann reaction. The results thus far obtained would seem to indicate that syphilis plays little or no part in the etiology of this disease. Sobernheim[89] has recently examined 4 cases of ozena of long standing in which evidences of very recent syphilitic infection were present. The cases, as would be expected, gave a positive reaction. The same writer had previously tested 17 cases of ozena in all of which the results were entirely negative. Weinstein[90] obtained only negative results in examining 8 cases of ozena and the same results were found by Alexander[91] in a series of 26 cases.

86. Busch, H.: Wassermannsche Seroreaktion bei nervöser Schwerhörigkeit und Otosklerose, Beitrage Ohres, Nase, Halses, 1909, iii, 42.

87. Beck, O.: Ueber die Erkrankungen des inneren Ohrs und deren Beziehungen zur Wassermannschen Serumreaktion, Monatschr. f. Ohrenh. u. Laryngo-Rhinol., 1910, xliv, 28.

88. Fowler, E. P.: The Serodiagnosis of Syphilis in Its Relation to Disease of the Ear, Ann. Otol., Rhinol. and Laryngol., 1910, xix, 367.

89. Sobernheim, W.: Ozaena und Syphilis: Neue Beobachtung, Arch. f. Laryngol. u. Rhinol., 1909, xxii, 430.

90. Weinstein, J.: Ueber die Bedeutung der Wassermannschen Syphilisreaktion für die Rhino-Laryngologie, Deutsch. med. Wchnschr., 1909, xxxv, 1696.

91. Alexander, A.: Serodiagnostische Untersuchungen zur Frage der Beziehungen zwischen Ozaena und Syphilis, Ztschr. f. Laryngol., 1909, i, 669.

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Additional light has been thrown on the intensely interesting problems of syphilitic heredity by recent investigations with the Wassermann reaction. Knoepfelmacher and Lehndorff[92] in examining 116 apparently healthy mothers of syphilitic children, found positive reactions in 62 per cent. of the cases, corroborating the work of the others that had been done in this direction. The inference might be drawn that the mothers were suffering from latent syphilis, a fact which might offer an explanation of Colles' law. That the inference is not to be drawn from the results of the Wassermann reaction alone has been set forth by Baisch.[93] He also found a large proportion of his reactions in apparently healthy mothers of syphilitic infants, and thinks that such findings might be explained on theoretical grounds in three ways. In the first place, the mothers might have been victims of latent syphilis. In the second place, the mothers might have been healthy, the positive reaction being due to inhibitory substances that had been produced in the child and passed through the dividing wall of the placenta into the mother's circulation. In the third place, the mothers might have been immune to syphilis, assuming that the inhibitory substances represent immune bodies produced in either fetal or maternal organism and circulating in the mother's blood. To settle the question Baisch combined the serologic examination of the mother and child with examinations for the *Spirochæta pallida* in the placenta. He found in these clinically healthy women, giving a positive Wassermann reaction, that the spirochetes could be found in both fetal and maternal portions of the placenta as well as in the maternal circulation, apparently proving the first possibility, namely, that the mothers were the bearers of latent syphilis.

92. Knoepfelmacher, W., and Lehndorff, H.: Das Collesche Gesetz, Med. Klin., 1909, v, 1506.

93. Baisch, K.: Die Vererbung der Syphilis auf Grund serologischer und bacteriologischer Untersuchungen, München. med. Wchnschr., 1909, lvi, 1920.

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Speaking further for this explanation and against the possibility of the reaction being due to inhibitory bodies passing from the child to the mother, is the fact that the positive reaction in the mother does not disappear after the birth of the child. Furthermore, the reaction can be positive in the mother and negative in the child. Bruck has pointed out that a number of cases have been reported in which a syphilitic child gave a negative reaction at birth, and later when manifestations appeared the reaction became positive. In spite of this the mother at the time of the birth gave a positive reaction. In these cases a passage of the inhibitory bodies from child to mother was certainly impossible. The most difficult cases to explain would be the ones in which the mothers, in addition to being clinically healthy, gave a negative reaction while their offspring were shown to be undoubtedly syphilitic from demonstration of the presence of the spirochetes. It might be thought that in these cases we had to deal with pure paternal heredity, or the explanation might be found in the failure of the Wassermann test to show a positive reaction. The proof that the explanation lay in the failure of the test was apparent from the fact that in the negative as in the positively reacting mothers, spirochetes were found in both portions of the placenta and in the maternal circulation.

Not only may our ideas concerning Colles' law have to be revised, but also those concerning the law of Profeta, which says that apparently healthy children of syphilitic parents are immune to syphilis, at least up to the time of puberty. The presence of a positive Wassermann reaction in a large number of these supposedly healthy children goes far to prove that here again the immunity to syphilis is only apparent.

That not only hereditarily syphilitic infants but also older children suffering from hereditary syphilis give a higher proportion of positive reactions has been shown

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by Bertin and Gayet.[94] In examining 25 undoubted cases of hereditary syphilis they found positive reactions in all but one case. Knoepfelmacher and Lehndorff[95] also conclude that older heredo-syphilitic children give a positive Wassermann reaction more often than adults in the late stage of acquired syphilis.

The results obtained by the Wassermann test in studying the relationship of idiocy to syphilis do not entirely agree. From an examination of 200 cases Kellner, Clemenz, Bruckner and Rautenberg[96] found only 3 per cent. of positive reactions and conclude that syphilis does not play an important etiological rôle in idiocy. Lippmann,[97] who found 13.2 per cent. of positive reactions, thinks that syphilis is not to be considered as the cause of idiocy, even though it is safe to regard some forms of this condition as syphilitic. Atwood[98] in the study of 204 idiots (employing the Noguchi modification) found a positive reaction in 14.7 per cent. of the cases. Plaut from his experience is unwilling to draw any conclusions as to the relationship of idiocy to syphilis.

In their serologic investigations on dementia præcox, Roubinovitch and Levaditi[99] obtained only negative results and conclude that the cerebral changes characterizing this condition are not due to syphilis. In an examination of 109 cases of locomotor ataxia Frey[100] found 69 per cent. of positive reactions, and thinks that

94. Bertin and Gayet: Syphilis héréditaire et réaction de Wassermann, Rev. de méd., 1910, xxx, 395.

95. Knoepfelmacher, W., and Lehndorff, H.: Untersuchungen heredoluetischer Kinder mittels der Wassermannschen Reaktion, Das Gesetz von Profeta, Wien. med. Wchnschr., 1909, lix, 2230.

96. Kellner, Clemenz, Bruchner and Rautenberg: Wassermannsche Reaktion bei Idiotie, Deutsch. med. Wchnschr., 1909, xxxvi, 1827.

97. Lippmann, H.: Ueber den Zusammenhang von Idiotie und Syphilis, München. med. Wchnschr., 1909, lvi, 2417.

98. Atwood, C. E.: Idiocy and Hereditary Syphilis, THE JOURNAL A. M. A., Aug. 6, 1910, p. 464.

99. Roubinovitch and Levaditi: Rôle de la syphilis dans l'étiologie de la démence précoce, Compt. rend. Soc. de biol., 1909, lxvi, 880.

100. Frey, E.: Die Wassermannsche Reaktion und ihr Wert bei der Diagnose der Tabes, Pest. med.-chir. Presse, 1910, xlvi, 116.

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it can be affirmed from these results that tabes is a parasyphilitic disease.

The value of the Wassermann reaction for pathologic-anatomic diagnosis would appear to be still in some doubt in spite of several favorable contributions to the subject that have recently appeared. Seligman and Blume[101] found the reaction positive in 8 cases of mesaortitis productiva, in 3 cases of flat base of the tongue and in 7 out of 8 cases of aneurism. They consider the method to be an aid to pathologic-anatomic diagnosis. Glaser and Wolfsohn[102] conclude from autopsy findings that the Wassermann reaction can give a correct diagnosis where neither history nor clinical manifestations show evidence of syphilis. The reaction was found positive by Schlimpert[103] in cases of mesaortitis (Heller), testicular nodes, flat tongue base and paresis. He states that the specificity of the reaction was in general upheld. In an examination of 100 cases Veszprémi[104] found 46 positive reactions, in 38 of which the reaction was justified by the post-mortem findings. None of the negative cases showed any evidence of syphilis. Examinations of pericardial, ascitic and hydrocele fluid and thoracic transudate gave practically the same results as when blood serum was used. Very unfavorable results were on the other hand obtained by Krefting,[105] who found 24 positive reactions in cases in which syphilis could probably be excluded. He therefore concludes that the Wassermann test with cadaver blood can give misleading results.

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101. Seligmann, E., and Blume, G.: Die Luesreaktion an der Leiche, Berl. klin. Wchnschr., 1909, xlvi, 1116.
102. Glaser, F., and Wolfsohn, G.: Klinische Beobachtungen uber die Wassermann-Neisser-Brucksche Reaktion und deren Kontrolle durch Sektionsresultate, Med. Klin., 1909, v, 1731.
103. Schlimpert, H.: Beobachtungen bei der Wassermannschen Reaktion, Deutsch. med. Wchnschr., 1909, xxxv, 1386.
104. Veszprémi, D.: Die Bedeutung der Wassermannschen Reaktion bei pathologisch-anatomischen Obduktionen, Centralbl. f. allg. Path. u. path. Anat., 1910, xxi, 193.
105. Krefting, R.: Leichensera und die Wassermannsche Syphilisreaktion, Deutsch. med. Wchnschr., 1910, xxxvi, 366.

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Finally it may be of interest to call attention to some recent serologic investigations tending to show the widespread infection of prostitutes by syphilis. Dreyer and Meirowsky[106] found the Wassermann reaction positive in 83 per cent. of prostitutes showing no clinical manifestations of syphilis. When the more delicate modification of Stern was used, the proportion was increased to nearly 90 per cent., Seligmann and Pinkus[107] have also found positive reactions in 88 per cent. of prostitutes giving no history or symptoms of syphilis.

In conclusion it would seem that there has been some very substantial progress during the past year in the serum diagnosis of syphilis. The continued investigations on the Wassermann test have not only added much that is new to our knowledge, but have tended to confirm the view that the reaction is one of very great practical value. The results obtained in a number of other diagnostic tests for syphilis must at least be considered as encouraging.

SUMMARY

1. The various precipitation tests for the diagnosis of syphilis are too unreliable to be of much practical value.

2. The Schürmann color reaction has been extensively tried and found to be worthless.

3. The favorable results that have been claimed for the intradermic reaction are at least encouraging, as the performance of the test seems to be simple.

4. Excellent results have been claimed by Richard Weil for his cobra venom test. They are, however, somewhat lessened in value by the fact that very considerable experience is required to perform the reaction.

106. Dreyer, A., and Meirowsky, E.: Serodiagnostische Untersuchungen bei Prostituierten, Deutsch. med. Wchnschr., 1909, xxxv, 1698.
107. Seligmann, E., and Pinkus, F.: Beitrage zur Theorie und Praxis der Wassermannschen Reaktion, Ztschr. f. Immunitätsforsch, 1910, v, 377.

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5. Further investigations are required to show whether the leuko-diagnosis, the antitryptic index or the meiostagmin reaction can be used as diagnostic aids in syphilis. The results obtained with the Much-Holzmann reaction appear to be of no value.

6. The artificial antigens of Sachs and Rondoni, and of Schürmann for the Wassermann reaction have not succeeded in replacing the use of organ extracts.

7. The use of barium sulphate suggested by Wechselmann to remove the disturbing complementoids from the patient's serum has apparently given a greater proportion of positive reactions than those obtained by the original Wassermann method.

8. The use of urine in place of serum for the Wassermann reaction is not to be recommended.

9. No single modification has as yet entirely replaced the original Wassermann method. The modifications of Hecht and of Stern have apparently given good results abroad, while the Noguchi test has received almost universal recognition in America. The methods of Bauer and of Tschernogubow (second test) appear to be of much less value.

10. To the list of non-syphilitic diseases which at times give a positive Wassermann reaction, must apparently be added lupus erythematosus acutus. It has also been found that many cases give a positive reaction following ether narcosis.

11. The diagnostic value of a positive reaction is generally recognized. There is no general agreement as yet regarding the value of the test as a guide for treatment.

12. From recent serologic investigations it would appear that syphilis plays a very important rôle in the etiology of aortic insufficiency. Syphilis is probably of more importance in the causation of nerve-deafness than has been previously supposed. There is apparently little or no relation between syphilis and ozena.

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13. A new field seems to have been opened by the Wassermann reaction for the discussion of the problem of the inheritance of syphilis and of the interpretation of the laws of Colles and Profeta.

14. In the field of pathologic-anatomic diagnosis the Wassermann reaction seems to be of considerable value.

15. Serologic examinations have shown that the percentage of syphilitic infections in prostitutes is extremely high.

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DISCUSSION ON PELLAGRA

At the St. Louis Session, the Section on Dermatology devoted Wednesday and Thursday mornings to the presentation of cases of pellagra and the discussion of that disease.

WEDNESDAY MORNING SESSION

DR. R. P. PRICE, Nevada, Mo.: I take pleasure in presenting two patients, both inmates of State Hospital No. 3, Nevada, Mo. They were treated for some time before we were aware of the character of the disease. The first case began with malaise and loss of appetite, followed in a short time by diarrhea and stomatitis and inflammation of the backs of the hands; there was also a small girdle extending around the wrists. These symptoms were treated symptomatically with little avail. I put the patients on iron, quinin and strychnin, Fowler's solution, with fruits and lemonades every two hours. This seemed to clear up the symptoms for a while; however, they returned in two or three weeks. The second patient has been in the hospital a little more than a month. The only symptom on admission was an inflammation on the backs of the hands. The diagnosis of her mental condition was maniac depressive insanity. She has run a subnormal temperature throughout the entire course. At this time she has developed diarrhea and stomatitis. I have two other cases at the hospital which developed in the same wards that these patients were in.

DR. A. RAVOGLI, Cincinnati: Pellagra is most commonly observed in Italy among the poorer classes and has been called a disease of poverty. It is supposed to be due to the fact that during certain seasons of the year these people are compelled to subsist on decayed or unripe maize which takes a greenish appearance. This, in many families, forms the staple article of food during the winter months. Under the microscope, this unripe green maize shows a peculiar fungus which has been called *Sporisorium maydis*, and it is to this that the occurrence of pellagra has been attributed. These patients after a time take an aversion to this article of food, and complain of burning of the throat. This is

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followed by gastric and intestinal symptoms, usually diarrhea. This constitutes, practically, the first stage of the disease. Afterward, there is an erythema of a deep, brownish color, affecting the backs of the hands and the forehead and neck—usually the parts exposed to the sun. The eruption becomes scaly in character and disappears in the cold weather, leaving atrophic scars. This skin manifestation is characteristic of the disease. These patients usually improve during the summer, when the quality of their food is better. In the more advanced cases the mental faculties begin to fail, and many of these patients commit suicide, usually by drowning. Others die of some complication or from the intestinal symptoms colliquative diarrhea. The prognosis of the disease in the early stage is not so bad, and I have seen many patients improve under better hygienic surroundings and tonic treatment. In the later stages, the prognosis is absolutely bad and only death can relieve the patients from their miserable condition.

Dr. James W. Babcock, Columbia, S. C.: We are all inclined to regard pellagra as a new disease in this country. As a matter of fact, it was reported in the United States as far back as 1864, and since then it has been observed in many institutions. Cases have now been reported from 28 states. It is prevalent in some of the asylums in California, and recently a number of cases have been found among the inmates of Blockley Hospital, Philadelphia. To-day, pellagra in this country presents a very momentous question. As to the etiology of the disease, I do not think that Americans are quite prepared to accept the maize origin of the disorder. The theory that it is due to a specific infection by a parasite has been advanced notably by Sambon of London and the strong resemblance that has been noted between this disease and sleeping sickness is suggestive that it is communicated by a gnat or sand-fly. One of the striking features of the American type of pellagra is its high mortality. In Alabama, in one asylum, the mortality was 68 per cent. In one of the public institutions in Columbia, South Carolina, out of 605 admissions, 92 had pellagra, a percentage of 15. Another interesting feature is the variety of mental symptoms shown by these patients. They are usually described as those of melancholia, although they may manifest themselves in many forms, from simple neurasthenia to manic-depressive insanity, and may even simulate general paresis of the insane. It has been truly said that when we know what pellagra is, we may have a much better understanding of insanity itself.

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DR. WILLIAM T. CORLETT, Cleveland: The cases of pellagra that I have seen in this country have been of a severe type; much more severe than I have seen in other countries. Most patients here find their way into asylums, while in some foreign countries, notably the West Indies and Egypt, one sees more cases outside of institutions—in short, there the affection seems less severe. In this regard it may correspond to many other diseases which at first, when new in a country, manifest themselves in a more severe type. As to the distribution of the disease in this country, in Ohio we have had one case of pellagra, so far as is known, and in the clinics of the large American cities, men who are familiar with the disease have not reported it, except in one or two instances. This shows that pellagra in America is mainly confined to certain localities. In the recognition of the disease, we must remember that pellagra is a constitutional disorder, and that one cannot with safety make a diagnosis from one symptom alone. Many cases of pellagra, even those shown here, although in one the skin lesions are typical, could scarcely be recognized from the cutaneous lesions alone. Other skin eruptions, such as simple erythema, inflammation, or eczema, may resemble the skin lesions of pellagra so closely that even the most skilled are liable to be mistaken. In the first case shown to-day, the condition of the mucous membranes is also typical, but the simple pigmentation of the skin is not sufficient to rest a diagnosis on, because it may be due to various causes. I have a colored photograph of a case of eczema which might well be mistaken for pellagra, but in my case we have only cutaneous symptoms.

Dr. Ravogli has stated that the poorer classes in Italy subsist largely during certain seasons of the year on damaged corn, and this has long since beeen advanced as the chief etiologic factor of pellagra. In this country, however, so far as we can trace, the disease is not limited to communities where corn is freely used as an article of diet. We have no positive proof thus far that Indian corn is responsible for the disease in this country. It may be that the use of corn in large quantities predisposes to the disease, but we are not in a position to condemn Indian corn as the sole etiologic factor of pellagra.

DR. JAMES W. BABCOCK, Columbia, S. C.: Pellagra in this country, is by no means confined to institutions, nor is it limited to the poorer classes. A number of cases have been reported among well-to-do people. The disease, so far as we know, is not communicable in the ordinary sense of

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that word, although there are instances in which several members of the same household were affected. There is no doubt that there is an extraordinary relationship between pellagra and insanity. Preexisting insanity is apparently a predisposing factor. The skin lesions of pellagra are not confined to the exposed surface, and many of these patients have lesions about the thighs, vulva, and anus. Cases have been reported in which women who have been operated on for relief of neurasthenic conditions have immediately afterwards developed the lesions of pellagra. There is still a great deal of mystery about this disease. We have just learned enough about it to warn us not to be too dogmatic in our assertions regarding it. I have seen a few cases in which there was glandular enlargement; in a case which I saw recently the parotid was enlarged before the appearance of the dermatitis. It is claimed that the disease is always associated with neurotic symptoms, although these may not be pronounced. As to the time of its occurrence, there is no age limit: I have seen it in a child in arms and in very old people.

Dr. J. M. King, Nashville: We do not know how pellagra is transmitted, nor whether the germ is a fungus or a protozoon. With reference to communicability we have had some very interesting cases in the south. In one institution, a Baptist orphanage, 17 cases have developed, the disease being introduced by a child 3 years old. That child was a member of a family of four, and all four later developed the disease. Following this, 12 or 13 other children in the institution became similarly affected. Whether the mode of transmission is by a fly or some other insect or through the food, we do not know. In the country, several miles from Nashville, a woman developed the disease, and shortly afterward her husband became similarly affected. In another case, the disease was apparently transmitted by the washing of clothes and I have heard of several instances in which the disease affected two persons who were intimately associated. In the family of a Methodist minister the wife and daughter contracted the disease in rapid succession. I have seen the disease among the very best classes—white people in the better walks of life. In treatment, for the stomatitis I have found that a solution of silver nitrate, from 10 to 15 grains in glycerin and water, together with applications of peroxid of hydrogen, gave the best results, and internally I give a tonic mixture of iron, quinin and strychnin. This treatment should, of course, be combined with good food and a hygienic environment.

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Of the 17 cases that developed in the Baptist orphanage, 2 patients have died, and one is now in the terminal stages of the disease. The others are at least temporarily free from the disease. From the observation of our cases and the post-mortem findings, we have come to the conclusion that this is primarily a disease of the alimentary tract. The skin becomes so susceptible to the rays of the sun that an erythema is produced. I recently saw one patient who had the disease for 2 years, and in whom the skin manifestations did not appear until a week or so before death. It is unquestionably a constitutional disorder, and probably of gastro-intestinal origin. The diagnosis rests on the skin lesions and the patient's mental condition.

DR. JOHN D. LONG, Washington, D. C.: During the past few months, I have been making some studies and observations of pellagra in South Carolina, and have been particularly interested in the microscopic findings in the stools of pellagrins, namely, muscle fibers, starch, crystals of various kinds, fats, oils, mucus, pus, blood, vegetable cells and fibers, and parasites, such as amebas, flagellates, ascaris, uncinaria, trichuris, oxyuris, etc. These findings are of interest in connection with the possible etiology of the disease. I was inclined to believe that the disease was due to some intestinal toxin, and this view was strengthened by the fact that in the milder cases, those that were not too far advanced, the mental symptoms were relieved very markedly by free elimination through the intestinal tract. In the more advanced cases the patients were actually insane did not respond so well to treatment. The result of x-ray findings in these cases showed the presence of a number of spinal deposits, with pressure on certain spinal nerves and consequent interference with the function of those nerves. The presence of these spinal deposits was verified in one case which we had an opportunity to examine post-mortem.

THURSDAY MORNING SESSION

DR. GEORGE A. ZELLER, Superintendent State Hospital, Peoria, Ill.: It is due to the courtesy of the Governor and the Board of Administration of the State of Illinois that I am able to show these seven cases of pellagra. In 1908, roundly speaking, about 1,000 cases of pellagra were reported in this country; in 1909, 5,000 were reported, and this year the number seems to be increasing in the same proportion. The disease is characterized by slow but constant extension. It has been known in Italy for over a century and a half,

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and has been the object of careful study there by Lombroso and others. In the patients brought here this morning, the pigmentation of the skin, especially on the backs of the hands, which is usually very characteristic of the disease, is not very pronounced at this season of the year. While it is not believed that pellagra in this country has existed in the past to the same extent as it does now, still there were probably many cases that went unrecognized, especially in public institutions, and in retrospect now we see that in the insane patients in whom we had to apologize for the condition of the hands and arms we were really dealing with cases of pellagra. The public is gradually waking up to the importance of this disease, and in Great Britain, the king has recently appointed a commission to study the spread of the disease throughout the empire. The Governor of the State of Illinois has also appointed a commission, headed by Dr. Frank Billings. Many who have given this subject their consideration are taking a middle ground between the unconcerned and the alarmists. I represent the latter. I really feel that the situation is alarming. These patients have been brought here for study and instruction. All has been officially declared insane, and they have been in the hospital for varying lengths of time. In these patients, at present, the intestinal symptoms are lacking, but they will come later.

Pellagra (Italian, *pelle*, skin, and *agra*, rough) was first described by Frapolli in 1771. It has also been known as Alpine scurvy and sunstroke of the skin. It has been confused with leprosy, eczema of the hands and other cutaneous affections. Many unsuspected cases have recently been discovered in various public institutions. The U. S. Government, through Captains Siler and Nichols of the War Department and Dr. C. H. Lavinder, of the Public Health and Marine-Hospital Service, is now investigating the subject abroad, and Dr. John D. Long, of the latter service, has been pursuing investigations along similar lines in the South. In a city of 75,000 people, I recently saw a woman who had this disease for 7 years. She had been treated, at various times, by 12 physicians for supposed eczema and other conditions. Finally, she consulted a physician who had seen some of these cases at our institution, and he was able to make a correct diagnosis. She died recently with an undisputed history of the disease dating back 7 years. There are doubtless many similar cases in various cities throughout this country—cases of pellagra that have gone

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unrecognized, and the disease may be extending gradually, as has beeen the experience in Italy. Illinois was the fifteenth state in this country to report pellagra, and since then, cases have been reported from ten additional states. There has been some talk of a national congress for the study of pellagra this summer, but I question whether this would be an opportune time for such a meeting. I think it would be better to wait until the men who are studying the disease abroad are prepared to give us the results of their investigations, and in the meantime those men who have the opportunity should take up this work as a special study and learn what they can in regard to this mysterious malady.

As to the treatment of pellagra, we have had the best results with arsenic. On the theory that the causative factor of the disease was intestinal and due to the presence of a parasite or ameba, it has beeen suggested that the bowels be flushed through an appendicostomy wound, but so far nothing has been done along that line.

Dr. James W. Babcock, Columbia, S. C.: Dr. Zeller and I can tell you frankly that anyone who shows special interest in pellagra, or who tries to direct the attention of the medical profession to this important subject, is going to be criticized not only by the laity, but by our own profession as well. In the South Carolina asylum there were last year 605 admissions, and of these, 92 patients had pellagra, and because I have attempted to call attention to the importance of this subject, a brother physician, a fellow member of the South Carolina State Medical Society—who happened to be also a member of the state legislature, announced before that body that "Babcock is crazy on pellagra."

The subject of pellagra is a momentous one, particularly to the alienist. Two and a half years ago it was generally unrecognized in the United States. We are frequently told that it is a new disease, but when we look back to the musty records of the past, we find that 2 cases were reported by asylum physicians as far back as 1864; one by Dr. Tyler, of Somerville, Mass., and one by Dr. John P. Gray, of Utica, N. Y. Dr. W. J. W. Kerr, now of Corsicana, Texas, who was assistant physician of the Andersonville Prison during the Civil War, is satisfied that one of the causes of the mortality in that institution was due to pellagra. In 1883 a case was put on record by Dr. Samuel Sherwell of Brooklyn, N. Y. Subsequent to that, other cases were reported again by Dr. Sherwell and by Dr. Harris of Georgia. The first epidemic was reported by Dr. George H. Searcy, of

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Alabama, in 1907, who discovered a number of cases in the state insane asylum for negroes at Mt. Vernon, and in the same year I independently reported the presence of pellagra cases in the South Carolina Hospital for the Insane. Since then, patients suffering from this disease have been found in many other asylums, and to-day we have records of pellagra cases in 28 states, including California, where the disease is believed to have existed in one institution for the past 7 years. I have no doubt that there are at least 5,000 cases of pellagra scattered throughout this country, from the Atlantic to the Pacific, and from the lakes to the gulf. If I did not know from personal experience what unkind things have been said of physicians who have directed attention to this subject, I should be unwilling to admit that one medical man would raise his voice in criticism of another who is making an effort to emphasize the importance of the situation we are facing to-day. If pellagra has existed in this country for some years why was it not recognized earlier? Simply because the great medical authorities told us that it was an Italian disease. Osler, in the edition of his "Practice of Medicine" prior to the latest, says that pellagra has never been observed in the United States. I know a brother physician who recognized pellagra in the South Carolina penitentiary in the eighties, but abandoned his diagnosis for lack of authority from the medical writers he consulted. Five years ago, at a meeting of the South Carolina State Medical Society, an unmistakable case of pellagra was brought before one of the very best diagnosticians in the United States; he studied the case for an hour and then said the patient had "glossitis." Yet, in the face of all this, we are told that we are crazy about pellagra; but after a physician has seen patients die of this prevalent and loathsome but unrecognized disease. and at last thinks that he has light upon a dark subject, he is bound to raise his voice in warning in regard to this insidious and fatal malady. Let me say in passing that Dr. Walter Wyman, the head of the U. S. Public Health and Marine-Hospital Service more than anyone else in the United States, deserves our gratitude for the manner in which he has taken hold of the pellagra problem. He was broad-minded enough and strong enough to say, in 1908. "Yes, we will investigate this disease," and he has never taken a backward step, although, like the rest of us, he has doubtless been subjected to criticism for the continued activity he has shown. Captains Siler and Nichols of the U. S. Army have also been very active in the matter.

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Dr. Marcus Haase, Memphis, Tenn.: My experience with pellagra has been limited to 23 cases last year, and 6 cases so far this year. They have all been outside patients—not institutional cases. They either came to the hospital, or else I saw them in consultation outside with their physicians, and they were not cases in which the mental symptoms were pronounced. Of the 23 patients whom I saw in 1909, 5 died. The age of the youngest of my patients was 3 years, and the oldest was 70. I would hesitate to make the diagnosis in these cases from the skin lesions alone: other symptoms are necessary for a diagnosis. As to the causative factor in these cases, the corn theory has not been taken into consideration at all, excepting that cereals have been excluded from the diet of these patients.

Dr. Tinsley Browne, Hamilton, Mo.: I wish to report a case of pellagra that occurred in Northwestern Missouri, of about 3 years' standing. It was the first case of the kind I had seen, and I did not know what it was. The patient's hands first broke out with what was supposed to be sunburn. Then he developed an uncontrollable diarrhea and gradually became insane. The eruption on the hands recurred the following year. The man was a dentist, 55 years old, and had been a great user of the corn products.

Dr. Oliver S. Ormbsy, Chicago: The commission appointed by the Governor of the State of Illinois to investigate pellagra is engaged in various ways getting information both clinical and experimental but has nothing to report as yet. During the winter while the disease has been in abeyance. the work has been directed largely toward investigation of the corn and other food products. There is a special hospital at Kankakee where pellagra patients are kept under observation and it is hoped to accomplish something in this study. We all feel greatly indebted to men like Dr. Zeller and Babcock who through their enthusiasm and knowledge have awakened both the official and lay public to the importance of the subject and thereby made such an investigation possible. In regard to the diagnosis of pellagra, some mistakes have of course been made. Cases of eczema and other skin conditions have been erroneously diagnosed as pellagra. When this subject first came up, physicians visited the hospitals and saw these patients, and then went over the records, thinking that perhaps some cases might have escaped notice, but in this respect their experience was different from what it had been in connection with other new diseases. In the early experience, in blastomycosis, for example, we were able to recall unrecognized cases in the past, and the same is

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true of sporotrichosis, but it was not so of pellagra. We could not find the record of a single case in the past that we felt sure was an example of this disease.

Dr. Howard Fox, New York: It is perhaps presumptuous for a New York man to discuss pellagra on this occasion as in New York we have seen almost no cases of the disease. The interest which pellagra has excited among physicians in New York was shown at one of our meetings last fall when Dr. Babcock and Dr. Watson read papers on the subject. Reference has already been made to the two cases that have been seen and reported by Dr. Samuel Sherwell of Brooklyn. Dr. C. H. Lavinder has also seen a case at the Marine-Hospital on Staten Island. Another case of pellagra has been seen at Ward's Island and still another recently at Newark, New Jersey. The subject is of particular interest to me from its dermatologic aspect. From the descriptions in the text-books and especially from the excellent volume of Ludwig Merk there is no question in my mind that many of the cases seen in this country are identical with the cases of pellagra abroad.

Dr. Isadore Dyer, New Orleans: I had the privilege of studying the cases of pellagra which were investigated by Dr. Searcy during the first outbreak which was noted in this country, and which was, perhaps, the chief cause of inciting interest in this unusual disease. Since then, the city of New Orleans has produced a considerable group of cases of pellagra derived from the neighboring cities and located in the Charity Hospital. Comparatively few cases have occurred in the State of Louisiana proper. There are two insane asylums under the public direction, and in both of these a number of cases have been observed in the past few years. The statement that pellagra exists in this country I wish to endorse as a dermatologist, and say that in my opinion, it is a new disease. The first case I saw was sent to me by a country physician of Alabama who recognized it as pellagra. This was prior to the study of the Mount Vernon cases by Dr. Searcy. I did not concur in the diagnosis of the case sent, regarding the condition as a toxic erythema and treating it as such. This patient ultimately recovered, which strengthened me in my belief that the disease was not pellagra. My later observations of other similar cases led me to change my opinion of this original case, and to accept the diagnosis of the country physician that the case was one of pellagra. In regard to the care of this disorder, my experience has been limited to about 10 cases. I have seen patients in New

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Orleans in various stages of the disease, largely under the direction of Dr. Bass, who has done a great deal of work in connection with pellagra in Louisiana, and who has observed more cases than any one else in the city.

I am not an alarmist in relation to pellagra; I am a conservative. I believe that this is a disease which may be cured, and I am prompted to make this statement from my own results. In some of my cases, the disease was so far advanced that the patients made their own diagnosis. While there are certain skin diseases which are liable to be confused with pellagra, I differ with those who claim that the skin lesions of this disease are not distinctive and cannot be differentiated from ordinary sunburn. While there are atypical cases which it would be difficult to recognize, there are classical cases in which the skin lesions are characteristic In my investigation of this disease, which has beeen limited. I have learned to class these cases as belonging to the erythema group, and the internal or other evidences which they present argue in favor of that belief. I consider a persistent erythema limited to the hands, neck and chest as almost as strong a diagrammatic confirmation of pellagra as are the lesions of leprosy or those of tubercular syphilis. In the treatment of all my cases of pellagra I have used quinin hydrobromate, and even in advanced cases, with stomatitis and diarrhea, I have often given 10 grains 3 times daily, and have kept it up until those symptoms have been controlled. The dose can then be reduced. In addition, I have used arsenic, which I believe is of distinct service. None of my patients has died, and some are now free from the symptoms of the disease. I believe that quinin is of great service in the treatment and cure of pellagra.

Dr. A. J. Vance, Harrison, Ark.: Pellagra is described as a disease of Southern Europe, and until recently it has been considered foreign to our list of ills. The first report of the disease was in Spain in 1735, about 40 years after the introduction of Indian corn. Frapolli of Milan was the first to describe the disease and to call it pellagra in 1771. He declared it had existed since 1578, and since then Italy has been a hotbed for it. In 1884 the mortality was 13 per cent. In 1905 it had been reduced to 4.3 per cent. and in 1907 it had been still further reduced to 0.7 per cent. Marzari was the first to call attention in 1810, to the relationship between the use of corn and pellagra. Vincenzo Setti in 1826, asserted the main cause of pellagra to be a fungus growth on the corn, producing decomposition of the oils in the corn. In 1776, an ordinance was passed in Venice prohibiting the sale of corn having a bad taste or odor.

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There is nothing to indicate that pellagra is caused by corn *per se*, but by corn not fully matured and which has been stored in damp places and allowed to mold.

With the limited experience of physicians in the United States, the prognosis is considered grave. Statistics are meager and unsatisfactory, based on asylum cases which give a mortality of 67 per cent. of the patients, 10 per cent. become insane and these rarely ever recover. Pellagra is essentially a chronic condition. Pellagrins are said to live from 20 to 30 years. The disease is also liable to recur months after recovery seems to be complete, and death frequently follows the second or third attack. In addition to the eruption on the dorsal surface of fingers and hands which is very much like sunburn, we find diarrhea, sick stomach, stomatitis, and ulcers on mucous curfaces, in mouth, rectum and vagina; later the patient is nervous and probably delirious.

Has Dr. Babcock observed a peculiar odor of the feces so characteristic that a diagnosis can be made? Dr. Cole of Mobile has been getting good results from the transfusion of blood from cured pellagrins, and even from healthy persons who have never had pellagra. If Dr. Babcock and Dr. Zeller are crazy on the subject of pellagra, we should be thankful for such insanity. This is a serious problem, one which many of us will be required to meet.

Dr. James W. Babcock, Columbia, S. C.: Physicians are waking up to the fact that pellagra is a big subject, and to the asylum physician it is a different problem from what it is to the dermatologist. To the asylum physician it is a very serious question. We deplore the notoriety the subject has received through the newspapers, and we are willing to admit that there is at present in this country more or less pellagraphobia. Still, it may not after all be entirely unfounded. Dr. J. D. Long recently visited Blockley Hospital in Philadelphia, in consultation with the local staff and among the patients there he recognized 9 cases of pellagra, and 16 suspects. This shows that the disease is gradually being observed north of Mason and Dixon's line. Some French authorities have stated that there were probably only certain classes that were susceptible to this unknown toxin, those who eat maize, alcoholics and the insane. Dr. Vance referred to the peculiar odor of the stools of these patients. There may be some grounds for this belief, and I know nurses who state that such is the case. There is perhaps as much foundation for it as for the belief that smallpox has a peculiar and characteristic odor.

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DISCUSSION ON BLASTOMYCOTIC DERMATITIS

At the Friday morning clinical session, Dr. M. F. Engman, St. Louis, presented a patient with blastomncotic dermatitis.

ABSTRACT OF DISCUSSION

Dr. A. Ravogli, Cincinnati: There is certainly no doubt about the diagnosis of this case. I have now under my care a patient with these blastomycotic lesions in the gluteal regions and on the face and hands, and the bones have also become affected in the form of abscesses. The diagnosis from the clinical appearance of the lesions is impossible, while the microscopic diagnosis is comparatively easy. As regards the etiology, in the case I have referred to, the patient was a butcher by occupation, and in a case which I reported before the Ohio State Medical Association the man was a dealer in sheep's hides. I have given potassium iodid in large doses without resulting benefit. I treat my cases by washing the lesions with 1 to 1,000 bichlorid of mercury, scraping with the curette the granulomatous proliferations. Stubborn lesions I expose to the *x*-ray. In advanced cases, with general smyptoms, nothing can be done.

Dr. J. B. Kessler, Iowa City, Iowa: Dr. Ravogli states that he has used potassium iodid in blastomycotic dermatitis without resulting benefit. Four years ago, at a meeting of this section in Atlantic City, I reported a case of this kind in which the eruption was on the cheeks, forehead and shoulders. The patient was a nursing infant and recovered when the mother and child were put on potassium iodid. That child still remains in a healthy condition, with large scars as the only evidence of her dermatoses.

Dr. J. M. King, Nashville: Three or four years ago I had a case in which the lesions involved the back of one hand and extended down over the fingers. The entire back of the

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hand was curetted and then cauterized with phenol, followed by applications of alcohol and hot water to check the bleeding. A wet bichlorid dressing was then applied under oiled silk and the parts were subsequently exposed to the *x*-ray to the extent of producing a mild dermatitis. That patient was cured, and is well to-day. The diagnosis was confirmed microscopically by Dr. Litterer.

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DISCUSSION ON THE SCAPHOID SCAPULA

At the Friday morning clinical session, the subject of "The Clinical Recognition of the Scaphoid Type of Scapula and of Some of Its Correlations," was taken up by Dr. William W. Graves, St. Louis, who showed a number of boys with the scaphoid type of scapula, and made some remarks on the subject. He referred to his article, then in the printer's hands, which subsequently appeared in THE JOURNAL of the A. M. A., July 2, 1910, page 12.

ABSTRACT OF DISCUSSION

DR. A. JACOBI, New York: I would like to ask Dr. Graves what his reasons are for making the diagnosis of arteriosclerosis in these cases? By arteriosclerosis we understand a thickening of the arterial coats, usually of the intima. We expect to find it in hereditary syphilis—but even there it is absent in many instances and very rarely in the young—in chronic alcoholism, chronic nephritis, and still more rarely in chronic aortitis, or in excessive adiposity. When we have a case of arteriosclerosis in the adult, no matter whether it is an indication of advancing age, or of syphilis or of anything else, we look for the evidences of it; the changes in the various organs. That is why it is so commonly associated with Bright's disease and apoplexy. In young patients we have always been taught that it was often the result of inherited syphilis; and there, as in adults, we get the usual symptoms, including increased blood-pressure, which is found in almost every case.

DR. IRA C. CHASE, Fort Worth: I have been somewhat interested in the subject of embryology, and I would like to call your attention to the imperfect development of the shoulder girdle of these boys posteriorly, which impresses me as an evidence of degeneration.

DR. A. RAVOGLI, Cincinnati: I am glad to have my attention called to these cases and to this peculiar form of scaphoid

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scapula as a possible indication of hereditary syphilis. In the third generation, syphilis usually manifests itself in the form of malformations, such as missing fingers or in the faulty appearance of the vault of the palate, or as hare-lip. This is due, to a large extent, to the condition of the blood-vessels, which are usually the first to be affected, in the form of endoarteritis obliterans.

Dr. Julius Grinker. Chicago: I congratulate the city of St. Louis on having a man in the medical profession who sees when he looks. We have all probably seen this peculiar type of scapula, but have attached no significance to it. Henceforth, in the neurologic field, I will make it a point to examine every child that comes under my observation for this particular deformity or sign of degeneration, if such it be, and if it proves to be an indication of inherited syphilis it will be of value in connection with many types of cerebral palsy and imbecility.

Dr. Albert E. Sterne, Indianapolis: I think we ought to know something more definite about the previous clinical histories of these boys. It is not uncommon to see changes in the blood-vessels after severe general infections, such as measles, scarlet fever and diphtheria, and I believe that these acute diseases of childhood may have some significance in the production of certain physical changes, not including, perhaps, this peculiar deformity of the scapula. Dr. Graves has most carefully investigated this subject, as anyone who has seen and studied his numerous dissections of the scapular region, in series from early fetal life onward, can readily understand. His conclusions, therefore, are worthy of serious consideration, though we may not as yet be prepared to agree with him as to the scaphoid scapula being invariably an evidence of syphilis of the progenitors.

Dr. William W. Graves, St. Louis: I have gone very carefully into the embryology of the scaphoid scapula and have traced it back to the sixth week of fetal life. At this period the cartilaginous scapula has assumed that essential form it ever afterward maintains. This fact, in connection with the fact that it occurs in whole families and in such a large percentage of our population, caused me in my studies to draw but one definite conclusion, namely, nothing in the life of the individual after his birth can give him the scaphoid scapula. It is, therefore, either a congenital or a hereditary

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anomaly. I regard the scaphoid scapula as merely one of many manifestations of a general blight, since those having it deviate in many ways from average individuals. I do not doubt that another cause than syphilis in the ascendants would be found; I hope it will. But a patient study of many individuals and families, extending over a period of more than three and a half years, has revealed no other cause than syphilis in the ascendants.

The scaphoid scapula is correlated: first, with the characteristics of the whole individual; second, with certain conditions, such as nocturnal incontinence; third,, with a tendency to catarrhal affections and with adenoids; fourth, with an undue degree of lymph-gland palpability; and lastly, and above all, with a degree of vasculosclerotic changes out of all proportion to the years. With the aid of the Zapski binocular corneal microscope, such changes have been found in the conjunctival vessels of nursing infants whose parents have had a syphilitic infection, and by the ordinary methods of clinical examination in such progeny, I have been able to detect such changes as early as the fourth, and, as a rule, as early as the tenth year of life. Heretofore, we have not been in the habit of looking for signs of arteriosclerosis in children. We have thought of and searched for such changes, as a rule, after the thirtieth year of life.

I am glad that Dr. Jacobi has examined one of the boys presented and that his examination resulted in the confirmation of evidence of arteriosclerosis in this boy. Similar evidence would be found in each boy presented, and as a rule in children of syphilitic parentage. In my studies I have not failed to make use of a blood-pressure apparatus and in such progeny I have found only slight, yet rather constant, elevation of pressure. I regard such an apparatus as of little value alone in determining the presence of vascular changes. It is merely confirmatory, but its absence by no means excludes the condition. Vasculosclerotic changes from the one pre-eminent clinical fact discernible in individuals who suffer from acquired syphilis and the one significant fact discernible in their progeny. In my first communication on the scaphoid scapla I referred to vasculosclerotic changes as a sort of connecting thread between the syphilitic and his progeny. I hope Dr. Jacobi and the members of the Section on Dermatology and the medical profession generally will become interested in the ramifications of the scaphoid scapula. There are

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many intricate problems associated with it which will require patient work on the part of many investigators before definite conclusions can be reached. Of one thing I feel certain however; that a consideration of the scaphoid scapula and its correlations and a more intensive study of syphilitic progeny and of syphilitic parents, especially in a comparative way, will lead to the solution of many obscure conditions in general and special pathology, and to a more complete recognition of the effects of syphilis in the individual affected, in his children and in his children's children. Furthermore, I believe that such studies will make us less certain of the curability of syphilis.

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A CASE FOR DIAGNOSIS; PROBABLY SYPHILIS

ROBERT H. DAVIS, M.D.
ST. LOUIS

Patient.—R. J. T., aged 57 gives the following history: He was in the U. S. Army during the Spanish war, and left Cuba in April, 1899. At this time, he suffered slightly with pharyngitis, and the examining army surgeon told him he had an ulcer on the pharynx of which he, though a physician, was unaware. There was no glandular enlargement, and the pharyngitis soon passed away. He had, however, been smoking Cuban cigars which are licked by the natives in the process of manufacture. When 19 years of age he had several small sores on the penis, which were diagnosed as herpes progenitalis, but, becoming frightened, he privately placed himself on small doses of calomel, t. i. d., for several months. No eruption or adenopathy appeared. In June, 1889, he began to feel pain above and in front of left ear, in the depression formed by the constant wearing of an army hat with a stiff edge. The pain lasted about two weeks, in spite of discarding the hat, and was succeeded by a red macule in the above mentioned location. This lesion became papular and gradually spread peripherally, clearing in the center, where an ivory white, atrophic scar remained. In a month this lesion was the size of a twenty-five cent piece. During the next four years, it spread very slowly, reaching the opposite side of the forehead in 1903. During these four years, different physicians were consulted, but no relief was obtained, and various diagnoses such as lues, ring-worm, and lupus vulgaris were ventured.

Finally, in 1906, on his own initiative, he commenced the use of a blue light, made by allowing the diffuse sunlight, collected by a large funnel to be focused, by a large lens, on his face, after passing through an aqueous solution of cupric sulphate. Rapid improvement followed this treatment until, after one year, the only active lesion was a spot on the right eyelid. He stopped the light treatment in August, 1907, and

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the spot on the right eyelid remained stationary until July, 1908, when a blow on this eye started an acute exacerbation, which spread rapidly over the entire scalp, and a large part of the face, destroying both eyelids. The resulting exposure of the corneæ caused ulcers which have resulted in blindness. He can distinguish light in one eye only.

Examination.—In June, 1909, he entered the Washington University Hospital, St. Louis, service of Dr. W. A. Hardaway, since which time he has been under my care. The condition at that time showed an ulcer, size of the palm, on the right side of the forehead, extending back on the crown of the head. This lesion had an elevated, frambesiform-like base, above the level of the surrounding skin, and exuded a whitish yellow pus. The entire scalp, except this ulcer, was a smooth, shining atrophic scar. Numerous small ulcers were scattered over the cheeks and the right external ear, and behind the latter. The eyelids were gone and on their sites were raw, red, exuding surfaces. There was in no place a grouping of the lesions, or a tendency to serpigenous or crescentic arrangement. There was no bone involvement, but the cartilage of the right ala of the nose had been partially destroyed and a cicatrix marked the location of the area lost. The general examination revealed nothing abnormal. The urine was normal.

Treatment.—Locally a soothing and antiseptic salve was applied and he was allowed to use his blue light, the effect of which, however, was much reduced according to his statement, since the acute exacerbation began. Examination was made for blastomycetes and proved negative. The Von Pirquet cutaneous reaction was also negative. The administration of iodids was early resorted to, in the form of the well known "black tonic" alternating with the syrup of hydriodic acid, but the occurrence of acute iodism prevented a greater dose than 7 grs. of potassium iodid daily, for any length of time.

Finally a Wassermann test was done, and the result was strongly positive! By this time, the large ulcer on the forehead was almost healed, but the ravages of the disease on the face were frightful, and, for the first time, the upper and lower lips became affected, showing great swelling and deep ulcerations. The ulcers about the right ear returned and there was a fresh appearance of small ulcers, from a quarter to a dime in size, on the left cheek. Injections of the cyanate of mercury, grs. 1/6, were begun one month ago. They are given

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subcutaneously in the back, one every alternate day. The improvement was marked and immediate, the smaller ulcers healing, and on the left cheek, coalescing in the process of repair, forming a long, slightly crescentic, raised edge. Unfortunately the lips are improving more slowly, and their condition tends to an easy salivation, which complication has several timse occurred, necessitating the temporary discontinuance of the injection at such times. There are no lesions in the mouth, or any where on the body or limbs. Small doses of potassium iodid are being given as far as the patient can assimilate them.

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A CASE OF BROMID ERUPTION

ROBERT H. DAVIS, M.D.
ST. LOUIS

Patient.—B. H. has been suffering from nervousness for the last nine months, following child-birth. About Feb. 1, 1910, she began taking bromids, 40 grs. daily. This was continued for two months. On March 27 small bullæ began to appear on the shins. They rapidly enlarged, became pustules and dried into thick crusts, which showed a raised red base, when removed.

Examination.—The bromids were at once discontinued, and on May 3 she came to the Jewish Dispensary, St. Louis, and was referred to me. The condition then was as above described, the lesions on the right shin being comparatively few. On the left shin they formed a patch the size of the hand, extending from the ankle almost to the knee. This patch was irregular in shape, composed of discrete and confluent lesions of the above-mentioned type, with many similar crusted areas surrounding the main patch. She compained of severe pain and vertigo, but was a pronounced neurasthenic.

Treatment and Course.—The eruption continued to appear for three weeks after coming to the dispensary, that is, for seven weeks after the discontinuance of the bromids. One lesion on the forehead and one on the right arm were the only ones appearing in any other situation than the shins. These lesions also quickly resolved, unlike those on the shins. For the past three weeks her improvement has been rapid under mild intestinal antisepsis, and an alum and lead acetate solution locally. The height of intensity of the eruption was about seven weeks after the discontinuance of the drug.

ABSTRACT OF DISCUSSION

DR. OLIVER S. ORMSBY, Chicago: This patient reminds me strongly of a group of cases reported by me last year in which the lesions were practically limited to the legs. This group of cases bore such a close resemblance to blastomycosis that that diagnosis was made even by men who were familiar

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with that disease. The lesions began as papulo-pustules, which spread, forming plaques, while healing in the center. All the cases eventually proved to be examples of bromid eruption. This appears to be of the same type, although it does not so closely resemble blastomycosis. There is no doubt that the bromids are capable of producing an eruption similar to this and limited to the legs.

Dr. Frank C. Knowles, Philadelphia: I recently had charge of a case of bromid eruption in a child, in which the outbreak consisted of three palm-sized patches, limited to the lower portion of the right leg. The eruption lasted for some weeks on stopping the drug, and was reproduced on several occasions by giving the bromid again.

Dr. J. M. King, Nashville: In private practice I have had two cases of bromid eruption, one in a woman in whom the lesions were limited to the anterior tibial region. She had been taking 15 grains of bromid three times daily. The lesions were not as large as in this case. My best results were obtained with peroxid of hydrogen after curettage of the lesions and wet bichlorid dressings. My second case was in a man, 45 years old, in whom the lesions were also limited to the anterior tibial region.

Dr. Julius Grinker, Chicago: I had a case in which the eruption followed the administration of 10 grains of the bromid, three times daily. The lesions, which were in the form of papules, followed by ulcerations, appeared six weeks after beginning the administration of the drug and disappeared within two weeks after discontinuing treatment.

Dr. R. H. Davis, St. Louis: In treatment of this case, I have limited myself to simple intestinal antiseptics, such as salol, and locally have prescribed an alum and lead acetate wash.

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THE EXTERNAL PREPARATIONS OF THE U. S. P. AND THE NATIONAL FORMULARY *

C. S. N. HALLBERG, Phm.D., M.D.
CHICAGO

THE U. S. PHARMACOPEIA

The external preparations of the U. S. P. comprise some 55 articles representing the following classes:

Unguenta	Linimenta
Cerata	Collodia
Suppositoria	Cataplasmæ
Oleata	Chartæ

Previous to the last revision these preparations were designed from a purely pharmacal standpoint: that is, the selection of the vehicle—the forming substance—was governed primarily by pharmaceutical considerations, so as to insure stable and otherwise superficially satisfactory preparations.

Having immediate charge of these preparations in the last revision, it was our good fortune to receive suggestions from many medical specialists, ophthalmologists, gynecologists and dermatologists, such as Dr. W. L. Baum of this Section, and the formulas for these preparations were for the first time revised on a therapeutic basis. Since they have proved uniformly satisfactory pharmaceutically, it might be well here briefly to consider these preparations according to their class-

* The author of this paper being now engaged in the revision of the U. S. P. and the N. F., desires physicians to report to him any criticism on these preparations particularly the newer ones taken from the British Codex and also any additions that might be sufficiently valuable or extensively used to warrant admission to either the U. S. P. or the N. F. Address C. S. N. Hallberg, 74 E. Twelfth Street, Chicago, Ill.

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ification and therapeutic groupings, in order to determine whether practice has demonstrated the correctness of the theoretic considerations on which they were severally formulated, and it is hoped that the fullest discussion and criticism may obtain among those who use these preparations.

UNGUENTA—OINTMENTS

Impalpable mixtures of medicinal agents and a fatty vehicle, soft solids, melting at the body temperature, intended for external application or inunction. They may be grouped therapeutically according to the function of their respective vehicles:

1. *Epidermatic.*—Non-penetrative, non-absorptive, protective, antiseptic, etc.

Vehicles: Soft paraffin (petrolatum, etc.).

PREPARATION	PRINCIPAL INGREDIENT	PROPORTION
Unguentum acidi borici—	boric acid	10%
phenolis—	phenol (carbolic acid)	3%
zinci stearatis—	zinc stearate	50%
hydrargri diluti—	mercury	33%

2. *Endermatic:* Semipenetrative or semiabsorptive emollient, nutritive, astringent, etc.

Vehicle: Animal or vegetable fats, oils or waxes—lard, suet, almond oils, hydrated wool fat.

PREPARATION	PRINCIPAL INGREDIENT	PROPORTION
Unguentum acidi tannici—	ac. tannic,	20%
aquæ rosæ—	rose water,	20%
belladonnæ—	ext. belladonna,	10%
chrysarobini—	chrysarobin,	5%
diachylon—	lead plaster,	50%
hydrargyri—	mercury,	50%
hydrargyri nitratis—	mercury nitrate,	10%
iodi—	iodin,	4%
iodoformi—	iodoform,	10%
picis liquidæ—	tar,	50%
potassii iodidi—	potass. iodid,	10%
stramonii—	ext. stramoni,	10%
sulphuris—	sulphur, washed,	15%
veratrinæ—	veratrin,	4%
zinci oxidi—	zinc oxid,	20%

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Vehicle: Hydrated wool fat and petrolatum, equal parts.

Unguentum hydrargyri ammoniati,	10%
hydrargyri oxidi flavæ,	10%
hydrargyri oxidi rubri,	10%

3. *Diadermatic.*—Penetrative or absorptive—systemic or constitutional.

Vehicle: Hydrated wool-fat:

Lanoleum hydrargyri—50 per cent., not official.

CERATA—CERATES

Mixtures of fats, waxes, sometimes resin, of hard consistence, softening by heat, readily spread on cloth, adhering to the part applied. To serve as protective dressing or to produce antiseptic, astringent or vesicating effects.

PREPARATION	PRINCIPAL INGREDIENT	PROPERTY
Ceratum—		protective.
camphoræ—	linim. camphor, 10%	antiseptic.
plumbi subacetatis—	liq., 20%	astringent.
resinæ—		discutient.
resinæ compositus—		discutient.
cantharides—	32%	vesicant.

EMPLASTRA—PLASTERS

Mixtures of medicinal agents with lead plaster, rendered pliable by admixture with rubber, hard solid, readily softening so as to be spread on cloth or fabric, adhering to the skin-part to which it is applied. To serve as protective or supportive or to exercise specific effects.

PREPARATION	PRINCIPAL INGREDIENT	PROPERTY
Emplastrum plumbi—	diachylon, lead oleate.	
adhesivum—	rubber, petrolatum, 2%	
belladonnæ—	ext. belladonna, 30%	anodyne.
capsici—	oleoresin capsicum	rubefacient.
hydrargyri—	mercury, 33%	alterative.
opii—	ext. opium, 6%	anodyne.
saponis—	soap, 10%	stimulant.

The plasters of the present Pharmacopeia, all containing adhesive plaster as the vehicle, easily prepared and readily spread, are a vast improvement over the former "pitch plasters." Being endermatic, they exert the action of the respective medicinal agents, in which respect they differ from the commercial rubber plasters which are simply adhesive, do not permit any penetrative effect and are therefore therapeutically inert.

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SUPPOSITORIA—SUPPOSITORIES

Mixtures of the medicinal substances and a fatty or gelatinous vehicle readily fusible at the body temperature and made into different shapes for introduction into the various orifices of the body.

Three different kinds as to size and shape of suppositories are official.

1. *Rectal.*—Cone-shaped, weighing 2 gm.; vehicle theobroma oil.

2. *Urethral.*—Pencil-shaped, weighing from 1 to 2 gm.; vehicle glycerinated gelatin or theobroma oil.

3. *Vaginal.*—Subglobular or ovoid, weighing from 4 to 10 gm.; vehicle glycerinated gelatin or theobroma oil.

There are, besides, glycerin suppositories gelatinized by soap to permit of being made into dosage form for facile introduction in the rectum, there to act as a solvent and thus produce prompt evacuation. The true suppositories, on the other hand, being analgous to ointments or cerates, present to the surfaces the most intimate admixture of the various antiseptic, astringent, anodyne, etc., agents for the most favorable action on the parts to which applied.

While the selection of theobroma oil as a vehicle for rectal suppositories cannot be improved on, a non-fatty vehicle is preferable for those intended for urethral and vaginal use. Glycerinated gelatin is therefore given the preference, although the choice of also using theobroma oil is left free to the practitioner.

The reason for this distinction in the vehicle for these different kinds of suppositories is based on the information of clinical observers that, while the rectal secretions are normally alkaline and therefore a fatty vehicle is appropriate, the secretions of the genito-urinary organs being normally acid, a fatty vehicle would be less desirable and hence the choice of a non-fatty vehicle would be better adapted to the mucous surfaces under such conditions.

The choice of glycerinated gelatin for this purpose leaves nothing to be desired from a pharmaceutic stand-

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point, the suppositories being soft and flexible and owing to the great proportion of glycerin contained (about 50 per cent.) retaining their solubility for any reasonable length of time. With the use of the official gelatinum glycerinatum, these suppositories are readily and quickly prepared, the only requirement being the variously shaped molds.

Whether or not this distinction in vehicle in the different kind of suppositories is really of therapeutic advantage has not been so far generally demonstrated, since seldom is any other vehicle than theobroma oil specified, no matter what kind of suppositories are required. It is hoped that this question will be discussed so that the Committee on Revision will have the benefit of the experience of clinicians.

OLEATA—OLEATES

The official oleates are formed by direct union of the base with oleic acid. They belong to the so-called "insoluble soaps." To the best of our knowledge oleates are only endermatic and not diadermatic; that is, they penetrate into the skin but do not pass through so as to have systemic effect. The following official are saturated oleates:

Oleatum hydrargyri—(25 per cent. Hg oxid).
Oleatum quininæ—(25 per cent. quinin alkaloid).

The following are solutions of alkaloidal bases in oleic acid in excess. In the first three olive oil is substituted for about one-half the amount of oleic acid. The advantage of this has been questioned and deserves clinical observation.

Oleatum atropinæ,	**2%**	**Oleatum veratrinæ,**	**2%**
Oleatum cocainæ,	**5%**	**Oleatum aconitinæ,**	**2%**

Zinc oleate is a fine dry powder of a soapy feel valuable as a mild antiseptic and astringent "dusting powder."

COLLODIA—COLLODIONS

Solutions of medicinal substances in collodion, a solution of pyroxylin in ether-alcohol, which being applied with a pencil quickly dries and leaves an impervious film.

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The following are official:

Collodium—	collodium flexile—	
acidi tannici—	(styptic),	20%
cantharidatum—	(blistering),	60%
iodatum—	iodized,	5%
collodium iodoformatum—	(iodoform),	5%
salicylatum comp.—	(corn collodium),	
tiglii—	(croton oil),	10%

THE NATIONAL FORMULARY

While not so important a work as the U. S. P., the National Formulary contains many preparations extensively used by physicians; and now is the time to make such additions and corrections as may be advisable, since its revision is now proceeding.

The following several classes of preparations for external or local use are included and it is the desire of the Committee to be informed by physicians of what criticism they would make on these various formulas; also what other preparations they would propose for admission.

GLYCEROGELATINA—GLYCERO-GELATINS

Medicinal agents incorporated with a 25 per cent. solution of gelatin in glycerin. Especially useful as a dressing where bandages are inadmissable. Prepared from the official gelatenum glycerinatum by simply incorporating the medicinal agent, first levigated with glycerin, with the melted glycerogelatin. The jelly is melted by placing the container in hot water, when it is applied with a camel's-hair pencil.

Glycerogelatinum—	acidi salicylici,	10%
	iodoformi,	10%
zinci durum—	firm zinc glycerogelatin.	
zinci mollis—	soft zinc glycerogelatin.	

PASTA DERMATOLOGICA—DERMATOLOGIC PASTES

Ointment-like mixtures of starch, dextrin, zinc oxid, calcium carbonate or sulphur, made into a paste with glycerin, soft soap, petrolatum, lard or other fat, with antiseptic or astringent agents.

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Pasta dextrinata—Equal parts dextrin, glycerin and water.

ichthyoli—	Unna—ichthyol,	25%
naphtholi—Lassar—	beta-naphthol,	10%
resorcinolis mitis—Lassar—	resorcinol,	10%
zinci—Lassar—	zinc—salicyl,	2%
zinci mollis—Unna—	soft zinc paste.	
zinci sulfurata—Unna—	sulphur præcip.,	10%

STILI DILUBILIS—UNNA PENCILS

Stilus acidi salicylic dilubilis,	10 per cent.
Stilus cocainæ dilubilis,	5 per cent.

UNG. RESORCINI COMP.

This ointment, containing resorcinol, zinc oxid and bismuth subnitrate, each 6 parts, and oil of cade 12 parts, is extensively employed. The preparation discolors, but when the oil of cade is replaced by oil of birch (ol. ruscae) 6 parts (instead of 12 parts) a superior ointment is obtained. The opinion of physicians is decided on this.

UNGUENTA EXTENSA—SALVE-MULLS

Medicated cerates to be spread on gauze for continuous application to avoid maceration.

Ung. extensum zinci,	10%
hydrargyri chloridi corrosivi,	2 per mille
salicylatum,	10%
creosoti salicylatum.	

The following ointments of the British codex may also be of service:

Unguentum capsici (24 per cent. capsicum infused).
creosoti, 10 per cent. petrolatum.
suprarenalin, 10 per cent. suprarenalin.

Petrolatum combined with ammonia soap is used as a vehicle under the following titles:

Petrolatum saporatum liquidum—liquid petrox.
Petrolatum saporatum spissum—solid petrox.

These are rarely used except as vehicles for various potent agents; iodin, phenol, etc. The Latin title is unwieldy and becomes more so when linked to a specific name.

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PAROGEN

Under the title "Parogen" the British Codex contains the following formula containing 50 per cent. less liquid paraffin (liquid petrolatum) than that of the present N. F.

Parogenum—parogen: Syn. liquid parogen; vaso-liniment; oxygenated paraffin. Liquid paraffin 40; oleic acid 40; alcohol ammon. (5%) 20. Mix and agitate until a clear solution is obtained.

Also the following combinations, all made with the liquid parogen:

Parogen chloroformi camphoratum—camphorated chloroform parogen.

Camphor 37.50; chloroform 25, dissolve, add parogen 37.50.

Parogenum creosoti—creosote parogen—

Creosote 5; parogen 95; mix them.

Parogenum empyreumaticum—empyreumatic parogen.

Oil of cade 25; parogen 75; mix them.

Parogenum eucalyptolis—eucalyptol parogen.

Eucalyptol 20; parogen 80; mix them.

Parogenum guaiacolis—guaiacol parogen.

Guaiacol 20; parogen 80; mix them.

Parogenum hydrargyri—mercury parogen.

Mercury 30; wool fat 15; triturate till metallic globules cease to be visible, then add thick parogen, 55.

Parogenum ichthamolis—ichthamol parogen.

Ammonium ichthosulphonate 10, parogen to 100, dissolve and strain after standing.

Parogenum iodi—iodin parogen.

Iodin 10; powder and triturate till dissolved in oleic acid 40; mix with liquid paraffin 40 per cent, then alcohol ammon. (5 per cent.) 10.

Parogenum iodi dilutum—diluted iodin parogen.

Iodin parogen 60; parogen 40; mix.

Parogen iodoformi deodoratum—deodorized iodoform paraffin.

Iodoform 3, eucalyptol 3, parogen to 100. Dissolve iodoform in the parogen by warming cautiously; then add the eucalyptol.

Parogenum mentholis—menthol parogen.

Menthol 2, parogen to 100; dissolve by warming cautiously.

Parogenum naphtholis—naphthol parogen.

Naphthol 10; parogen to 100; triturate till dissolved.

Parogenum picis—tar parogen.

Tar 25, parogen to 100; mix them.

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Parogenum salicylatum—salicylated parogen.
Salicylic acid 10, parogen to 100; powder and triturate till dissolved.

Parogenum sulphuris—sulphur parogen.
Sulphur subl. 3, linseed oil 37; dissolve by aid of heat; then mix with parogen to 100.

Parogenum sulphuris compositum—compd. sulphur parogen.
Sulphur parogen 10, oil of cade 10, thymol 0.3, eucalyptol 3, oil of turpentine 30, parogen to 100. Dissolve the thymol and eucalyptol in the oil, mix with the parogen.

Parogenum terebinthina—turpentine paraffin.
Venice turpentine fact. 20, parogen to 100; mix them.

Parogenum spissum—thick parogen.
Hard paraffin 12, liquid paraffin 48, oleic acid 30. alcohol ammon. (5 per cent.) 10. Melt the hard paraffin; add the liquid paraffin, then the oleic acid and the alcohol and continue the heat on a water-bath until the product weighs 90.

The following single generic names are suggested for the same reasons as was the parogenum for petrolatum saponatum. If physicians are expected to use these preparations, the generic titles must be composed of single words otherwise when the specific name is added they become too cumbersome.

LANOLIMENTA—LANOLIMENTS

Lanolimentum mentholis—menthol lanoliment.
Menthol 5, hydrous wool-fat to 100; mix.

Lanolimentum mentholis salicylatum—salicylated menthol lanoliment.
Menthol 5, methyl salicylate 10, hydrous wool-fat to 100; mix.

Paraffinoleum mentholis—menthol paraffinol—liquid petrolatum and menthol.
Menthol 2, liquid petrolatum to 100. Mix and strain if necessary.

Paraffinoleum eucalypti—eucalyptus paraffinol.
Oil eucalyptus 5, liquid petrolatum to 100; mix.

Paraffinoleum thymolis—thymol paraffinol.
Thymol 1, liquid petrolatum to 100. Dissolve by trituration in a warm mortar.

Paraffinol phenolis—phenol paraffinol.
Phenol cryst. 1, liquid petrolatum to 100. Dissolve by trituration in a warm mortar.

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A CHRONIC ITCHING PAPULAR ERUPTION OF THE AXILLA, PUBES AND BREAST

MARCUS HAASE, M.D.
Professor of Diseases of the Skin, College of Physicians and Surgeons, University of Memphis
MEMPHIS, TENN.

Dr. George Henry Fox,[1] in 1902, described a peculiarly localized papular eruption in the axilla that was extremely itchy and resisted all treatment. In the same article Dr. Fordyce reported the histologic findings in Dr. Fox's case, but at this time no attempt was made by either to classify the condition.

In a subsequent article[2] before the thirty-second annual meeting of the American Dermatological Society in 1908, Dr. Fordyce called attention to the lack of weight given by the American dermatologists to a group of skin diseases classed by Dr. Brocq under the term "lichenification," reported more in detail, both clinically and histologically, an additional case, and tentatively classed it among those eruptions to which Brocq has given the name *nervodermite chronique circonscrite.*

In reviewing this article, Dr. Colcott Fox,[3] after complimenting the author on his work, says: "We think many will hesitate to pronounce the condition a lichenification, as we know that state in this country."

It would seem from this that the British dermatologists, of whom Dr. Colcott Fox is one of the most pains-

1. Jour. Cutan. and Gen. Urin. Dis., January, 1902.
2. Am. Dermat. Soc., 1908, p. 118.
3. Brit. Jour. of Dermat., xxi, 269.

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Fig. 1.—Papular eruption in axilla.

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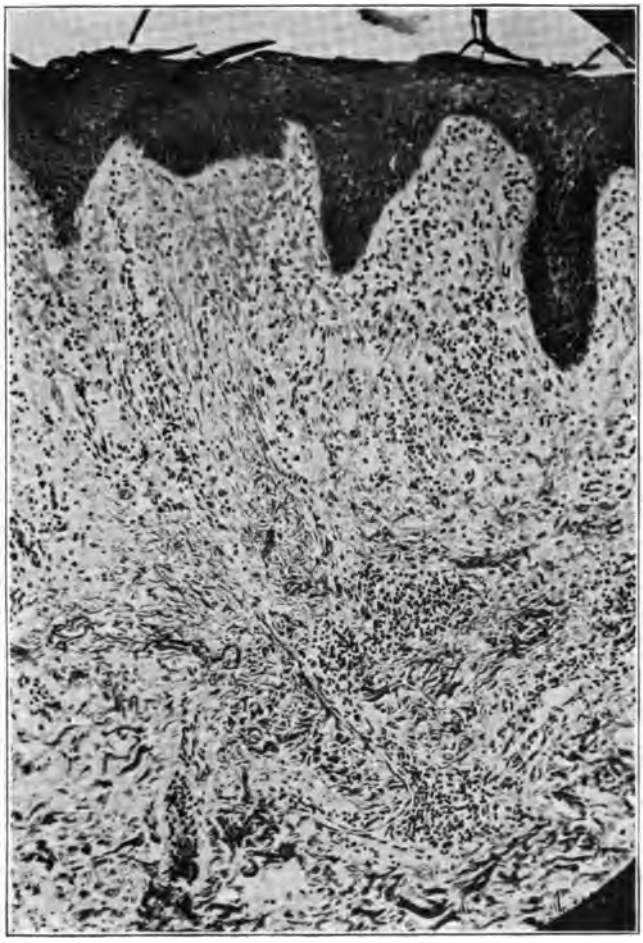

Fig. 2.—Edema of papillary layer of corium. Elastic fibers destroyed or so changed in character that they do not take characteristic stain.

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Fig. 3.—Destruction of the epidermal cells with vesicle formation.

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Fig. 4.—Epidermis showing hyperkeratosis, vacuole formation about nuclei and edema of the corium.

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taking clinicians and histologists, were as derelict as their American confrères in recognizing this identification of a class of skin diseases that assisted much in the simplification of the nomenclature of dermatology.

But Dr. Fordyce's classification has found a better reception in circles equally interested and no less critical, as I have seen a personal letter from Dr. Brocq to Dr. Fordyce, in which he entirely agrees with the latter that the affection in question is a lichenification and states that he has seen numerous similar cases in his practice. I have had under my observation for the past two years a case that is a clinical prototype of those reported by Drs. Fox and Fordyce.

History.—The patient is a young woman, aged 21, anemic and decidedly neurotic. Her family history is unimportant, her father having died at thirty-eight years of age of pneumonia. One brother died recently of pulmonary tuberculosis. Her mother, three sisters and two bothers are all in good health. Her past history is interesting in that she has had three distinct, severe attacks of hemoglobinuric fever at 12, 14 and 16 years of age. At 15 she contracted scabies, which lasted four or five weeks. From 14 to 17 years of age she suffered severely with periodical headaches, and the menses were not established until the latter year, and then appeared only at irregular intervals. The disease for which she consulted me, began at 17 years of age while attending school, as an intense itching in the axillæ. In three or four weeks the papules appeared, and she then noticed that the hairs in that region became brittle, and as she expressed it, "dropped off." The pubes became affected four months later in a similar manner, and not until a year later did the breasts become involved.

Examination.—When she came under my care, the disease was limited to the hairy portion of the axillæ and pubes, and about the nipples of the breasts. In the axillæ and over the pubes the eruption consisted of closely aggregated, round, smooth, firm papules, in size from a pin-head to a small pea, those in the pubic region being somewhat larger than in the axillæ. At the apex of each papule was a slight depression or a grayish plug. When the skin was put on a stretch the

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lines were markedly exaggerated, the papules occupying the ridge (Fig. 1). The color over the region affected was normal, or a pale pink. The lesions on the breasts were more discrete, there being not more than a dozen papules on either breast. These were deeper in color and about the size of a large pinhead. Alopecia was complete in the axilla and over the pubes. The itching was almost intolerable, frequently depriving the patient of sleep, and at times she would lose control of herself to the extent of having to be forcibly restrained by two of her sisters. It was always worse at night, and during and after any excitement, either pleasurable or otherwise. Repeated thorough examinations revealed no constitutional disturbance, blood and urine being negative.

Treatment.—Treatment in my case proved even less successful than in those previously reported. She was given innumerable antipruritics, with only temporary relief. Resorcin, pyrogallic acid, chrysarobin, and various tars, in increasing strength, were used, with no better results. The *x*-ray was very positively refused, but high-frequency currents were applied for over four weeks. Saline cathartics were administered for more than a month, as were salicin and phenyl salicylate, in increasing doses. In October, 1908, after she had been under my care for five months, the patient's condition became so deplorable that it was thought best to place her under the constant observation of nurses. For this purpose, she was sent to the Presbyterian Hospital, with a nurse in constant attendance. She was allowed from two to five hours outdoor exercise, all medication, both external and internal, having been stopped, except hot salt solutions applied to the diseased areas. Under this treatment she rested better, her mental condition improved and she gained some weight. When last seen, less than a month ago, the condition in the axilla and over the pubes showed little or no change. The papules were still present, the hair had not returned and the itching though less frequent was at times very annoying. The patient's mental condition had continued to improve, and she was devoting all her time to music and outdoor life. She still continued the use of the hot salt water packs.

Biopsy.—Sections made from a biopsy taken from the axillæ showed an extensive acanthosis, most marked about the sweat-duct, a dense hyperkeratosis at the mouth of the duct, in some instances extending deep into the duct proper. There was an extracellular and intracellular edema, with a shrinkage

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Fig. 5.—Hair follicle and epidermal projection enclosing sweat-duct with degeneration of cells. Cellular infiltration in foci in corium.

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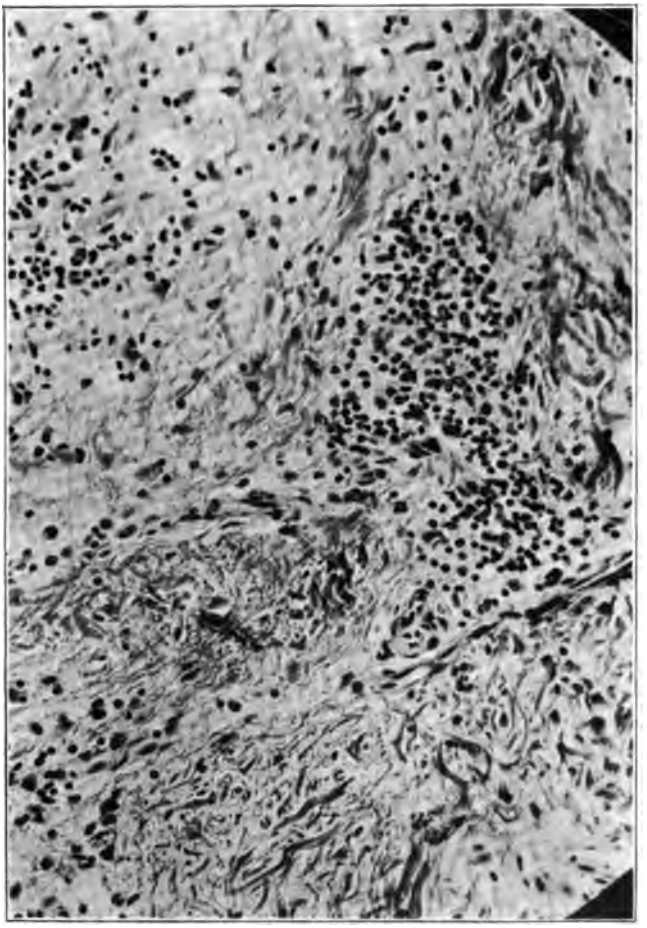

Fig. 6.—Character of cell infiltration in corium.

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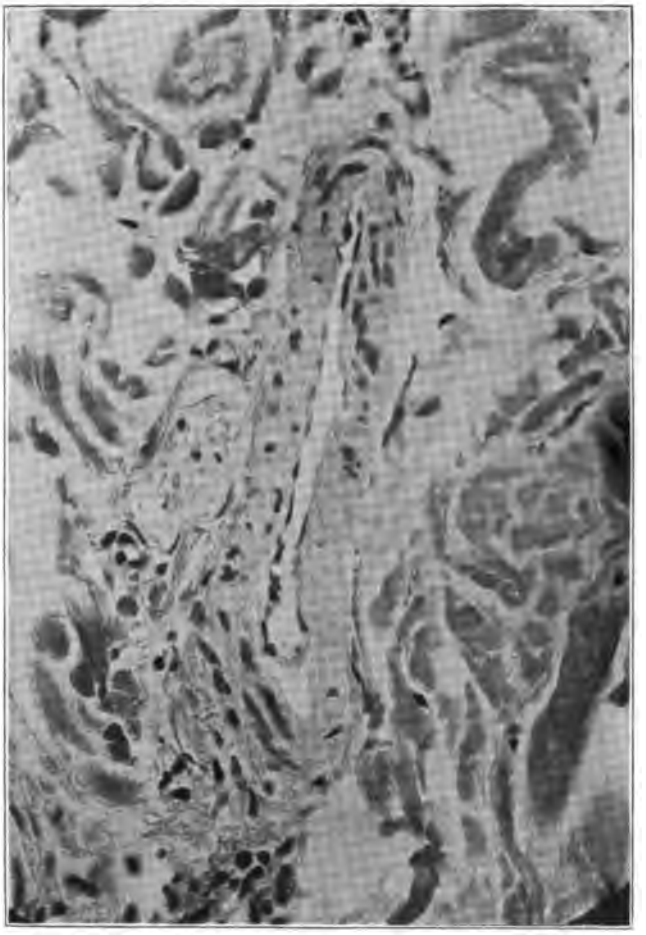

Fig. 7.—Hyaline degeneration of small artery in corium.

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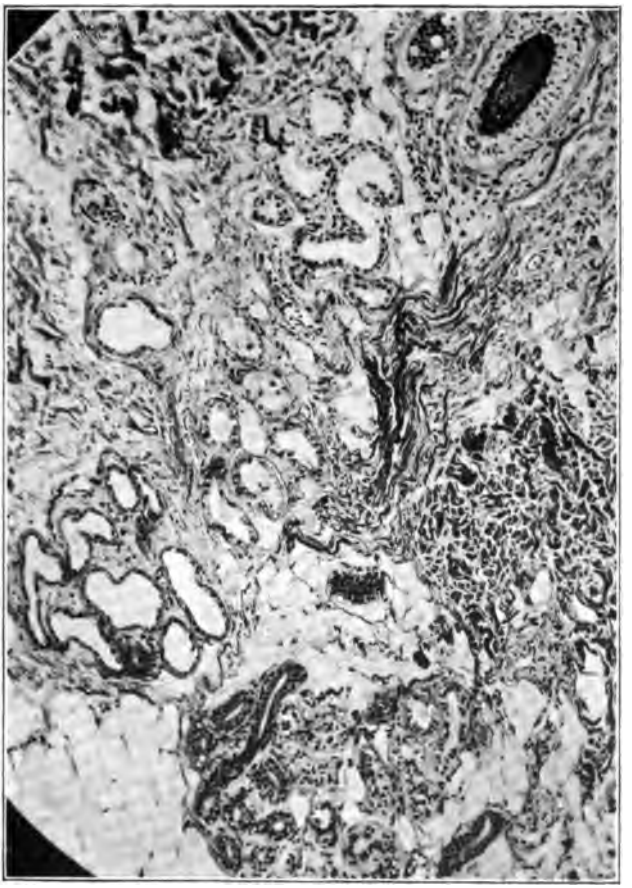

Fig. 8.—Degeneration of lining cells and dilatation of glands with adjacent apparently uninjured glands.

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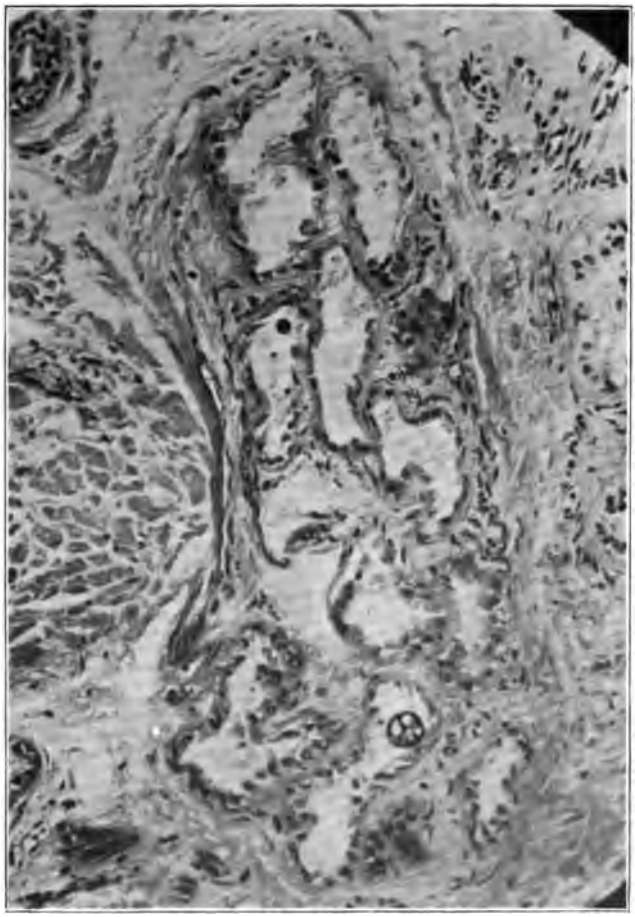

Fig. 9.—Dilatation of sweat glands showing partial casts. In two of the gland acini are concretions or bodies mentioned in text.

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of the nuclei seen throughout the prickle cells, and in places small vesicles had formed. In the papillary and subpapillary layers of the corium, a marked degeneration and edema were found, and the elastic tissue in this region was so changed that it did not take the usual stains. An infiltration of lymphocytes and plasma cells was present in foci and about the vessels and sweat glands. A hyaline degeneration was seen in some of the arteries of the corium, with an atrophy of the nuclei of the wall, but by far the most marked change was the dilatation of the sweat-gland accompanied with a degeneration of the lining cells. In some of the tubules, there were partial casts, and in two there were found round concretions or bodies the nature of which is to me obscure.

The histologic picture in my case differed only in minor details from that reported by Dr. Fordyce; namely, the hyaline degeneration of the arteries and the changes in the staining quality of the elastic fibers.

In conclusion, it is apparent that Dr. Fordyce's contention is well grounded, and that as his conclusions are approved by Brocq, we may accept this peculiarly localized dermatosis as a lichenification, the etiology of which is still in doubt.

If one might hazard a guess at the cycle of histologic changes occurring in the development of the disease, I would suggest that the pathologic condition began in the sweat-glands, with a morbid change in the lining cells, followed by a destruction of the cells and a dilatation of the gland proper, and that all other changes demonstrated were secondary to this process, and due to the elimination of a toxin yet unknown.

Memphis Trust Building.

ABSTRACT OF DISCUSSION

DR. J. A. FORDYCE, New York: Through the kindness of Dr. George H. Fox of New York I saw a third case of this affection in which the eruption occurred in the identical localities, and I have had personal communications with other physicians who have described similar cases. These observations might lead one to think that we have at least a distinct clinical picture if not a definite entity. As supporting the

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toxic origin of such a condition, we see on other parts of the skin purplish thickened patches made up of papules which have run together and which occur in individuals who are suffering from some toxemia. This toxemia may result from the excessive use of tea, coffee, or alcohol, or possibly a combination of these agents, with intestinal fermentation. In the cases which occur on other parts of the body than the axillary or pubic region I have been unable to demonstrate changes in the sweat glands, but subsequent investigation may show them.

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LIST OF MEMBERS OF THE SECTION ON DERMATOLOGY

List of present members of the American Medical Association who are making a specialty of dermatology and who have registered in this Section at one or more of the last five meetings. The numbers after the names indicate the record of attendance at annual sessions. (0 indicates 1910; 9, 1909, etc.)

Abercrombie, John R., 827 N. Eutaw St., Baltimore. 9.
Alderson, H. E., 937 Asbury St., San Francisco. 9.
Alderson, M. E., Russellville, Ky. 6, 9.
Alexander, T. B., Scituate, Mass. 6.
Allen, John Thomas, Brownsville, Tenn. 6.
Allen, Kotz, 195 Cox Ave., Memphis, Tenn. 0.
Anderson, A., 15 Walnut St., New Britain, Conn. 7.
Ankrim, L. F., 5014 Penn Ave., Pittsburg. 6, 8, 9, 0.
Anthony, H. G., 92 State St., Chicago. 2, 3, 4, 8.
Armstrong, L. W., Breckenridge, Minn. 8.
Aud, C. Z., Cecilian, Ky. 6.
Baer, C. A., 128 Wisconsin Pt., Milwaukee, Wis. 0.
Bathurst, Wm. R., 308 Southern Trust Bldg., Little Rock, Ark. 9, 0.
Baugh, A. W., Paoli, Pa. 8.
Baumann, Fred, 103 State St., Chicago. 8.
Baum, Henry Clay, 813 University Blk., Syracuse, N. Y. 6. 7, 8.
Baum, Wm. L., 103 State St., Chicago. 4, 6, 7, 8, 0.
Beard, Leslie A., Polo, Ill. 8.
Biddle, A. P., 57 W. Fort St., Detroit. 6, 8.
Bierhoff, Frederic, 10 W. 61st St., New York. 7.
Biggs, E. L., Hot Springs, Ark., 6.
Bishop, R. W., 70 State St., Chicago. 8.
Bobb, C. S., Mitchell, S. D. 8.
Boehm, Joseph L., 717 N. 8th St., St. Louis. 7. 8.
Boggs, Russell H., Empire Bldg., Pittsburg. 6, 7, 9.
Bookwalter, Harry, Columbiana, Ohio. 7.
Bower, G. B. M., Vernal, Utah. 8.
Bradley, Mark S., 36 Pearl St., Hartford, Conn. 6.
Brayton, A. W., 24 Kentucky Ave., Indianapolis. 3, 4, 6, 8, 0.
Breakey, J. F., 213 E. Huron St., Ann Arbor, Mich. 8.
Brosius, W. L., Gallatin, Mo. 0.
Brotherlin, Henry Hale, Hollidaysburg, Pa. 7.
Brown, F. W. A., Oshkosh, Wis. 8.
Brown, George S., Conway, Ark. 0.
Buehler, Geo. V., 1075 Boylston St., Boston. 6.
Bufford, John Henry, 1079 Boylston St., Boston. 6.
Bulkley, L. D., 531 Madison Ave., New York. 2, 3, 4, 6, 7, 9.
Bull, T. M., Naugatuck, Conn. 4, 7, 8.
Burns, F. S., 224 Marlborough St., Boston. 6.
Burt, J. C., Westinghouse Bldg., Pittsburg, Pa. 9.
Butler, G. E., Fall River, Mass. 6, 7.
Calvin, W. D., 235 W. Wayne St., Fort Wayne. 6.
Cameron, V. V., Marion, Ind. 8.
Campbell, R. R., 100 State St., Chicago. 2, 3, 4, 7, 8, 9.
Casselberry, C. M., 1069 Boylston St. Boston. 9.
Chipman, E. D., 240 Stockton St., San Francisco. 9.
Chrysler, Oscar, National Home, Wis. 8.
Clack, J. Morgan, Rockwood, Tenn. 6.
Cocks, E. L., 156 W. 119th St., New York. 2, 4, 6.
Cole, Albert M., 401 Newton Claypool Bldg., Indianapolis, Ind. 8
Collings, H. P., Dugan-Stuart Bldg., Hot Springs, Ark. 4, 0.
Collings, S. P. Dugar-Stuart Bldg., Hot Springs, Ark. 4, 7.
Cook, John W., Pendleton, Ind. 6.
Cook, Paul B., 603 Fairmount Ave., St. Paul, Minn. 8.

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Conaway, A. C., 30 E. Main St., Marshalltown, Ia. 0.
Corlett, Wm. T., 1935 Euclid Ave., Cleveland. 2, 4, 7, 8, 0.
Cornwell, Herbert C. de V., 173 Madison Ave., New York. 6.
Corwin, R. W., Pueblo, Colo. 7.
Courtney, Walter, Brainerd, Minn. 8.
Crume, G. P., 512 Nicollet Ave., Minneapolis. 8.
Cunningham, J. H. Jr., 829 Boylston St., Boston. 9.
Danielson, Karl A., Litchfield, Minn. 0.
Davis, Geo. W., 227 W. 12th St., Kansas City, Mo. 0.
Davis, R. H., 4500 Olive St., St. Louis, Mo. 0.
Davis, William H., 909 17th St., Denver, Colo. 6.
Day, C. R., 630 Security Bldg., Oklahoma City, Okla. 8.
Dean, Geo. R., Spartansburg, S. C. 7.
Dickson, J. A., Ashtabula, Ohio. 6
Dittrich, E. W., 158 E. 81st St., New York City. 8.
Dix, George A., 105 Pleasant St., Worcester, Mass. 6.
Doughty, James W., Ft. Stellacoom, Wash. 6.
Dorr, R. C., Batesville, Ark. 0.
Duncan, J. H., Humboldt Bldg., St. Louis, Mo. 0.
Dyer, Isadore, 124 Baronne St., New Orleans. 3, 4, 0.
Earle, Samuel T., Jr., 1431 Linden Ave., Baltimore. 6.
Eberhardt, Noble M., 72 Madison St., Chicago. 8.
Ellis, Leonard R., 366 Central Ave., Hot Springs, Ark. 8.
English, R. M., 17 West St., Danbury, Conn. 8.
Engman, Martin F., Humboldt Bldg., St. Louis, Mo. 9, 0.
Engsberg, Wm. A., Lake Mills, Wis. 8.
Erdman, Bernhard, 430 Newton Claypool Bldg., Indianapolis. 9.
Farrell, John T., 1488 Westminster, Providence, R. I. 7, 8, 9.
Fenyes, Adalbert, 55 E. Colorado St., Pasadena, Cal. 6.
Fewsmith, Joseph, 47 Central Ave., Newark, N. J. 6.
Field, Geo. J., Salt Lake City, Utah. 7. 0.
Finck, Edward Beecher, 1120 Girard St., Philadelphia. 6, 7, 8, 9.
Fischkin, E. A., 3037 Humboldt Blvd., Chicago. 8, 0.
Flynn, E. H., Marquette, Mich. 8.
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